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(54) Title: NOVEL COMPOUNDS

(57) Abstract: Polypeptides and polynucleotides of the genes set forth in Table I and methods for producing such polypeptides by recombinant techniques are disclosed. Also disclosed are methods for utilizing polypeptides and polynucleotides of the genes set forth in Table I in diagnostic assays.

Novel Compounds

Field of Invention

This invention relates to newly identified polypeptides and polynucleotides encoding such polypeptides, to their use in diagnosis and in identifying compounds that may be agonists, antagonists that are potentially useful in therapy, and to production of such polypeptides and polynucleotides. The polynucleotides and polypeptides of the present invention also relate to proteins with signal sequences which allow them to be secreted extracellularly or membrane-associated (hereinafter often referred collectively as secreted proteins or secreted polypeptides).

Background of the Invention

The drug discovery process is currently undergoing a fundamental revolution as it embraces "functional genomics", that is, high throughput genome- or gene-based biology. This approach as a means to identify genes and gene products as therapeutic targets is rapidly superseding earlier approaches based on "positional cloning". A phenotype, that is a biological function or genetic disease, would be identified and this would then be tracked back to the responsible gene, based on its genetic map position.

Functional genomics relies heavily on high-throughput DNA sequencing technologies and the various tools of bioinformatics to identify gene sequences of potential interest from the many molecular biology databases now available. There is a continuing need to identify and characterise further genes and their related polypeptides/proteins, as targets for drug discovery.

Proteins and polypeptides that are naturally secreted into blood, lymph and other body fluids, or secreted into the cellular membrane are of primary interest for pharmaceutical research and development. The reason for this interest is the relative ease to target protein therapeutics into their place of action (body fluids or the cellular membrane). The natural pathway for protein secretion into extracellular space is the endoplasmic reticulum in eukaryotes and the inner membrane in prokaryotes (Palade, 1975, Science, 189, 347; Milstein, Brownlee, Harrison, and Mathews, 1972, Nature New Biol., 239, 117; Blobel, and Dobberstein, 1975, J. Cell. Biol., 67, 835). On the other hand, there is no known natural pathway for exporting a protein from the exterior of the cells into the cytosol (with the exception of pinocytosis, a mechanism of snake venom toxin intrusion into cells). Therefore targeting protein therapeutics into cells poses extreme difficulties.

The secreted and membrane-associated proteins include but are not limited to all peptide hormones and their receptors (including but not limited to insulin, growth hormones, chemokines, cytokines, neuropeptides, integrins, kallikreins, lamins, melanins, natriuretic hormones, neuropsin, neurotropins, pituitiary hormones, pleiotropins, prostaglandins, secretogranins, selectins, thromboglobulins, thymosins), the breast and colon cancer gene products, leptin, the obesity gene protein and its receptors, serum albumin, superoxide dismutase, spliceosome proteins, 7TM (transmembrane) proteins also called as G-protein coupled receptors, immunoglobulins, several families of serine proteinases (including but not limited to proteins of the blood coagulation cascade, digestive enzymes), deoxyribonuclease I, etc.

Therapeutics based on secreted or membrane-associated proteins approved by FDA or foreign agencies include but are not limited to insulin, glucagon, growth hormone, chorionic gonadotropin, follicle stimulating hormone, luteinizing hormone, calcitonin, adrenocorticotropic hormone (ACTH), vasopressin, interleukines, interferones, immunoglobulins, lactoferrin (diverse products marketed by several companies), tissue-type plasminogen activator (Alteplase by Genentech), hyaulorindase (Wydase by Wyeth-Ayerst), dornase alpha (Pulmozyme\ by Genentech), Chymodiactin (chymopapain by Knoll), alglucerase (Ceredase by Genzyme), streptokinase (Kabikinase by Pharmacia) (Streptase by Astra), etc. This indicates that secreted and membrane-associated proteins have an established, proven history as therapeutic targets. Clearly, there is a need for identification and characterization of further secreted and membrane-associated proteins which can play a role in preventing, ameliorating or correcting dysfunction or disease, including but not limited to diabetes, breast-, prostate-, colon cancer and other malignant tumors, hyper- and hypotension, obesity, bulimia, anorexia, growth abnormalities, asthma, manic depression, dementia, delirium, mental retardation, Huntington's disease, Tourette's syndrome, schizophrenia, growth, mental or sexual development disorders, and dysfunctions of the blood cascade system including those leading to stroke. The proteins of the present invention which include the signal sequences are also useful to further elucidate the mechanism of protein transport which at present is not entirely understood, and thus can be used as research tools.

Summary of the Invention

The present invention relates to particular polypeptides and polynucleotides of the genes set forth in Table I, including recombinant materials and methods for their production. Such polypeptides and polynucleotides are of interest in relation to methods of treatment of certain diseases, including, but not limited to, the diseases set forth in Tables III and V, hereinafter referred to as "diseases of the invention". In a further aspect, the invention relates to methods for identifying agonists and antagonists (*e.g.*, inhibitors) using the materials provided by the invention, and treating conditions associated with imbalance of polypeptides and/or polynucleotides of the genes set forth in Table I with the identified compounds. In still a further aspect, the invention relates to diagnostic assays for detecting diseases associated with inappropriate activity or levels the genes set forth in Table I. Another aspect of the invention concerns a polynucleotide comprising any of the nucleotide sequences set forth in the Sequence Listing and a polypeptide comprising a polypeptide encoded by the nucleotide sequence. In another aspect, the invention relates to a polypeptide comprising any of the polypeptide sequences set forth in the Sequence Listing and recombinant materials and methods for their production. Another aspect of the invention relates to methods for using such polypeptides and polynucleotides. Such uses include the treatment of diseases, abnormalities and disorders (hereinafter simply referred to as diseases) caused by abnormal expression, production, function and or metabolism of the genes of this invention, and such diseases are readily apparent by those skilled in the art from the homology to other proteins disclosed for each attached sequence. In still another aspect, the invention relates to methods to identify agonists and antagonists using the materials provided by the invention, and treating conditions associated with the imbalance with the identified compounds. Yet another aspect of the invention relates to diagnostic assays for detecting diseases associated with inappropriate activity or levels of the secreted proteins of the present invention.

Description of the Invention

In a first aspect, the present invention relates to polypeptides the genes set forth in Table I. Such polypeptides include:

(a) an isolated polypeptide encoded by a polynucleotide comprising a sequence set forth in the Sequence Listing, herein when referring to polynucleotides or polypeptides of the Sequence Listing, a reference is also made to the Sequence Listing referred to in the Sequence Listing;

(b) an isolated polypeptide comprising a polypeptide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;

(c) an isolated polypeptide comprising a polypeptide sequence set forth in the Sequence Listing;

(d) an isolated polypeptide having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;

(e) a polypeptide sequence set forth in the Sequence Listing; and

(f) an isolated polypeptide having or comprising a polypeptide sequence that has an Identity Index of 0.95, 0.96, 0.97, 0.98, or 0.99 compared to a polypeptide sequence set forth in the Sequence Listing;

(g) fragments and variants of such polypeptides in (a) to (f).

Polypeptides of the present invention are believed to be members of the gene families set forth in Table II . They are therefore of therapeutic and diagnostic interest for the reasons set forth in Tables III and V. The biological properties of the polypeptides and polynucleotides of the genes set forth in Table I are hereinafter referred to as "the biological activity" of polypeptides and polynucleotides of the genes set forth in Table I. Preferably, a polypeptide of the present invention exhibits at least one biological activity of the genes set forth in Table I.

Polypeptides of the present invention also include variants of the aforementioned polypeptides, including all allelic forms and splice variants. Such polypeptides vary from the reference polypeptide by insertions, deletions, and substitutions that may be conservative or non-conservative, or any combination thereof. Particularly preferred variants are those in which several, for instance from 50 to 30, from 30 to 20, from 20 to 10, from 10 to 5, from 5 to 3, from 3 to 2, from 2 to 1 or 1 amino acids are inserted, substituted, or deleted, in any combination.

Preferred fragments of polypeptides of the present invention include an isolated polypeptide comprising an amino acid sequence having at least 30, 50 or 100 contiguous amino acids from an amino acid sequence set forth in the Sequence Listing, or an isolated polypeptide comprising an amino acid sequence having at least 30, 50 or 100 contiguous amino acids truncated or deleted from an amino acid sequence set forth in the Sequence Listing. Preferred fragments are biologically active fragments that mediate the biological activity of polypeptides and polynucleotides of the genes set forth in Table I, including those with a similar activity or an improved activity, or with a decreased undesirable activity. Also preferred are those fragments that are antigenic or immunogenic in an animal, especially in a human.

Fragments of a polypeptide of the invention may be employed for producing the corresponding full-length polypeptide by peptide synthesis; therefore, these variants may be

employed as intermediates for producing the full-length polypeptides of the invention. A polypeptide of the present invention may be in the form of the "mature" protein or may be a part of a larger protein such as a precursor or a fusion protein. It is often advantageous to include an additional amino acid sequence that contains secretory or leader sequences, pro-sequences, sequences that aid in purification, for instance multiple histidine residues, or an additional sequence for stability during recombinant production.

Polypeptides of the present invention can be prepared in any suitable manner, for instance by isolation form naturally occurring sources, from genetically engineered host cells comprising expression systems (*vide infra*) or by chemical synthesis, using for instance automated peptide synthesizers, or a combination of such methods. Means for preparing such polypeptides are well understood in the art.

In a further aspect, the present invention relates to polynucleotides of the genes set forth in Table I. Such polynucleotides include:

(a) an isolated polynucleotide comprising a polynucleotide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polynucleotide sequence set forth in the Sequence Listing;

(b) an isolated polynucleotide comprising a polynucleotide set forth in the Sequence Listing;

(c) an isolated polynucleotide having at least 95%, 96%, 97%, 98%, or 99% identity to a polynucleotide set forth in the Sequence Listing;

(d) an isolated polynucleotide set forth in the Sequence Listing;

(e) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;

(f) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide set forth in the Sequence Listing;

(g) an isolated polynucleotide having a polynucleotide sequence encoding a polypeptide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;

(h) an isolated polynucleotide encoding a polypeptide set forth in the Sequence Listing;

(i) an isolated polynucleotide having or comprising a polynucleotide sequence that has an Identity Index of 0.95, 0.96, 0.97, 0.98, or 0.99 compared to a polynucleotide sequence set forth in the Sequence Listing;

(j) an isolated polynucleotide having or comprising a polynucleotide sequence encoding a polypeptide sequence that has an Identity Index of 0.95, 0.96, 0.97, 0.98, or 0.99 compared to a polypeptide sequence set forth in the Sequence Listing; and

polynucleotides that are fragments and variants of the above mentioned polynucleotides or that are complementary to above mentioned polynucleotides, over the entire length thereof.

Preferred fragments of polynucleotides of the present invention include an isolated polynucleotide comprising an nucleotide sequence having at least 15, 30, 50 or 100 contiguous nucleotides from a sequence set forth in the Sequence Listing, or an isolated polynucleotide comprising a sequence having at least 30, 50 or 100 contiguous nucleotides truncated or deleted from a sequence set forth in the Sequence Listing.

Preferred variants of polynucleotides of the present invention include splice variants, allelic variants, and polymorphisms, including polynucleotides having one or more single nucleotide polymorphisms (SNPs).

Polynucleotides of the present invention also include polynucleotides encoding polypeptide variants that comprise an amino acid sequence set forth in the Sequence Listing and in which several, for instance from 50 to 30, from 30 to 20, from 20 to 10, from 10 to 5, from 5 to 3, from 3 to 2, from 2 to 1 or 1 amino acid residues are substituted, deleted or added, in any combination.

In a further aspect, the present invention provides polynucleotides that are RNA transcripts of the DNA sequences of the present invention. Accordingly, there is provided an RNA polynucleotide that:

(a) comprises an RNA transcript of the DNA sequence encoding a polypeptide set forth in the Sequence Listing;

(b) is a RNA transcript of a DNA sequence encoding a polypeptide set forth in the Sequence Listing;

(c) comprises an RNA transcript of a DNA sequence set forth in the Sequence Listing; or

(d) is a RNA transcript of a DNA sequence set forth in the Sequence Listing; and RNA polynucleotides that are complementary thereto.

The polynucleotide sequences set forth in the Sequence Listing show homology with the polynucleotide sequences set forth in Table II. A polynucleotide sequence set forth in the Sequence Listing is a cDNA sequence that encodes a polypeptide set forth in the Sequence Listing. A polynucleotide sequence encoding a polypeptide set forth in the Sequence Listing may be identical to a polypeptide encoding a sequence set forth in the Sequence Listing or it may be a sequence other than a sequence set forth in the Sequence

Listing, which, as a result of the redundancy (degeneracy) of the genetic code, also encodes a polypeptide set forth in the Sequence Listing. A polypeptide of a sequence set forth in the Sequence Listingis related to other proteins of the gene families set forth in Table II, having homology and/or structural similarity with the polypeptides set forth in Table II. Preferred polypeptides and polynucleotides of the present invention are expected to have, *inter alia*, similar biological functions/properties to their homologous polypeptides and polynucleotides. Furthermore, preferred polypeptides and polynucleotides of the present invention have at least one activity of the genes set forth in Table I.

Polynucleotides of the present invention may be obtained using standard cloning and screening techniques from a cDNA library derived from mRNA from the tissues set forth in Table IV (see for instance, Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 2nd Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1989)). Polynucleotides of the invention can also be obtained from natural sources such as genomic DNA libraries or can be synthesized using well known and commercially available techniques.

When polynucleotides of the present invention are used for the recombinant production of polypeptides of the present invention, the polynucleotide may include the coding sequence for the mature polypeptide, by itself, or the coding sequence for the mature polypeptide in reading frame with other coding sequences, such as those encoding a leader or secretory sequence, a pre-, or pro- or prepro- protein sequence, or other fusion peptide portions. For example, a marker sequence that facilitates purification of the fused polypeptide can be encoded. In certain preferred embodiments of this aspect of the invention, the marker sequence is a hexa-histidine peptide, as provided in the pQE vector (Qiagen, Inc.) and described in Gentz *et al.*, Proc Natl Acad Sci USA (1989) 86:821-824, or is an HA tag. A polynucleotide may also contain non-coding 5' and 3' sequences, such as transcribed, non-translated sequences, splicing and polyadenylation signals, ribosome binding sites and sequences that stabilize mRNA.

Polynucleotides that are identical, or have sufficient identity to a polynucleotide sequence set forth in the Sequence Listing, may be used as hybridization probes for cDNA and genomic DNA or as primers for a nucleic acid amplification reaction (for instance, PCR). Such probes and primers may be used to isolate full-length cDNAs and genomic clones encoding polypeptides of the present invention and to isolate cDNA and genomic clones of other genes (including genes encoding paralogs from human sources and orthologs and paralogs from other species) that have a high sequence similarity to sequences set forth in the Sequence Listing, typically at least 95% identity. Preferred probes and primers will

generally comprise at least 15 nucleotides, preferably, at least 30 nucleotides and may have at least 50, if not at least 100 nucleotides. Particularly preferred probes will have between 30 and 50 nucleotides. Particularly preferred primers will have between 20 and 25 nucleotides.

A polynucleotide encoding a polypeptide of the present invention, including homologs from other species, may be obtained by a process comprising the steps of screening a library under stringent hybridization conditions with a labeled probe having a sequence set forth in the Sequence Listing or a fragment thereof, preferably of at least 15 nucleotides; and isolating full-length cDNA and genomic clones containing the polynucleotide sequence set forth in the Sequence Listing. Such hybridization techniques are well known to the skilled artisan. Preferred stringent hybridization conditions include overnight incubation at 42°C in a solution comprising: 50% formamide, 5xSSC (150mM NaCl, 15mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10 % dextran sulfate, and 20 microgram/ml denatured, sheared salmon sperm DNA; followed by washing the filters in 0.1x SSC at about 65°C. Thus the present invention also includes isolated polynucleotides, preferably with a nucleotide sequence of at least 100, obtained by screening a library under stringent hybridization conditions with a labeled probe having the sequence set forth in the Sequence Listing or a fragment thereof, preferably of at least 15 nucleotides.

The skilled artisan will appreciate that, in many cases, an isolated cDNA sequence will be incomplete, in that the region coding for the polypeptide does not extend all the way through to the 5' terminus. This is a consequence of reverse transcriptase, an enzyme with inherently low "processivity" (a measure of the ability of the enzyme to remain attached to the template during the polymerisation reaction), failing to complete a DNA copy of the mRNA template during first strand cDNA synthesis.

There are several methods available and well known to those skilled in the art to obtain full-length cDNAs, or extend short cDNAs, for example those based on the method of Rapid Amplification of cDNA ends (RACE) (see, for example, Frohman et al., Proc Nat Acad Sci USA 85, 8998-9002, 1988). Recent modifications of the technique, exemplified by the Marathon (trade-mark) technology (Clontech Laboratories Inc.) for example, have significantly simplified the search for longer cDNAs. In the Marathon (trade mark) technology, cDNAs have been prepared from mRNA extracted from a chosen tissue and an 'adaptor' sequence ligated onto each end. Nucleic acid amplification (PCR) is then carried out to amplify the "missing" 5' end of the cDNA using a combination of gene specific and adaptor specific oligonucleotide primers. The PCR reaction is then repeated using 'nested'

primers, that is, primers designed to anneal within the amplified product (typically an adapter specific primer that anneals further 3' in the adaptor sequence and a gene specific primer that anneals further 5' in the known gene sequence). The products of this reaction can then be analyzed by DNA sequencing and a full-length cDNA constructed either by joining the product directly to the existing cDNA to give a complete sequence, or carrying out a separate full-length PCR using the new sequence information for the design of the 5' primer.

Recombinant polypeptides of the present invention may be prepared by processes well known in the art from genetically engineered host cells comprising expression systems. Accordingly, in a further aspect, the present invention relates to expression systems comprising a polynucleotide or polynucleotides of the present invention, to host cells which are genetically engineered with such expression systems and to the production of polypeptides of the invention by recombinant techniques. Cell-free translation systems can also be employed to produce such proteins using RNAs derived from the DNA constructs of the present invention.

For recombinant production, host cells can be genetically engineered to incorporate expression systems or portions thereof for polynucleotides of the present invention. Polynucleotides may be introduced into host cells by methods described in many standard laboratory manuals, such as Davis et al., Basic Methods in Molecular Biology (1986) and Sambrook *et al.*(*ibid*). Preferred methods of introducing polynucleotides into host cells include, for instance, calcium phosphate transfection, DEAE-dextran mediated transfection, transvection, micro-injection, cationic lipid-mediated transfection, electroporation, transduction, scrape loading, ballistic introduction or infection.

Representative examples of appropriate hosts include bacterial cells, such as *Streptococci*, *Staphylococci*, *E. coli*, *Streptomyces* and *Bacillus subtilis* cells; fungal cells, such as yeast cells and *Aspergillus* cells; insect cells such as *Drosophila* S2 and *Spodoptera* Sf9 cells; animal cells such as CHO, COS, HeLa, C127, 3T3, BHK, HEK 293 and Bowes melanoma cells; and plant cells.

A great variety of expression systems can be used, for instance, chromosomal, episomal and virus-derived systems, *e.g.*, vectors derived from bacterial plasmids, from bacteriophage, from transposons, from yeast episomes, from insertion elements, from yeast chromosomal elements, from viruses such as baculoviruses, papova viruses, such as SV40, vaccinia viruses, adenoviruses, fowl pox viruses, pseudorabies viruses and retroviruses, and vectors derived from combinations thereof, such as those derived from plasmid and bacteriophage genetic elements, such as cosmids and phagemids. The expression systems

may contain control regions that regulate as well as engender expression. Generally, any system or vector that is able to maintain, propagate or express a polynucleotide to produce a polypeptide in a host may be used. The appropriate polynucleotide sequence may be inserted into an expression system by any of a variety of well-known and routine techniques, such as, for example, those set forth in Sambrook *et al.*, (*ibid*). Appropriate secretion signals may be incorporated into the desired polypeptide to allow secretion of the translated protein into the lumen of the endoplasmic reticulum, the periplasmic space or the extracellular environment. These signals may be endogenous to the polypeptide or they may be heterologous signals.

If a polypeptide of the present invention is to be expressed for use in screening assays, it is generally preferred that the polypeptide be produced at the surface of the cell. In this event, the cells may be harvested prior to use in the screening assay. If the polypeptide is secreted into the medium, the medium can be recovered in order to recover and purify the polypeptide. If produced intracellularly, the cells must first be lysed before the polypeptide is recovered.

Polypeptides of the present invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography is employed for purification. Well known techniques for refolding proteins may be employed to regenerate active conformation when the polypeptide is denatured during intracellular synthesis, isolation and/or purification.

Polynucleotides of the present invention may be used as diagnostic reagents, through detecting mutations in the associated gene. Detection of a mutated form of a gene is characterized by the polynucleotides set forth in the Sequence Listing in the cDNA or genomic sequence and which is associated with a dysfunction. Will provide a diagnostic tool that can add to, or define, a diagnosis of a disease, or susceptibility to a disease, which results from under-expression, over-expression or altered spatial or temporal expression of the gene. Individuals carrying mutations in the gene may be detected at the DNA level by a variety of techniques well known in the art.

Nucleic acids for diagnosis may be obtained from a subject's cells, such as from blood, urine, saliva, tissue biopsy or autopsy material. The genomic DNA may be used directly for detection or it may be amplified enzymatically by using PCR, preferably RT-PCR, or other amplification techniques prior to analysis. RNA or cDNA may also be used

in similar fashion. Deletions and insertions can be detected by a change in size of the amplified product in comparison to the normal genotype. Point mutations can be identified by hybridizing amplified DNA to labeled nucleotide sequences of the genes set forth in Table I. Perfectly matched sequences can be distinguished from mismatched duplexes by RNase digestion or by differences in melting temperatures. DNA sequence difference may also be detected by alterations in the electrophoretic mobility of DNA fragments in gels, with or without denaturing agents, or by direct DNA sequencing (see, for instance, Myers *et al.*, Science (1985) 230:1242). Sequence changes at specific locations may also be revealed by nuclease protection assays, such as RNase and S1 protection or the chemical cleavage method (see Cotton *et al.*, Proc Natl Acad Sci USA (1985) 85: 4397-4401).

An array of oligonucleotides probes comprising polynucleotide sequences or fragments thereof of the genes set forth in Table I can be constructed to conduct efficient screening of *e.g.*, genetic mutations. Such arrays are preferably high density arrays or grids. Array technology methods are well known and have general applicability and can be used to address a variety of questions in molecular genetics including gene expression, genetic linkage, and genetic variability, see, for example, M. Chee et al., Science, 274, 610-613 (1996) and other references cited therein.

Detection of abnormally decreased or increased levels of polypeptide or mRNA expression may also be used for diagnosing or determining susceptibility of a subject to a disease of the invention. Decreased or increased expression can be measured at the RNA level using any of the methods well known in the art for the quantitation of polynucleotides, such as, for example, nucleic acid amplification, for instance PCR, RT-PCR, RNase protection, Northern blotting and other hybridization methods. Assay techniques that can be used to determine levels of a protein, such as a polypeptide of the present invention, in a sample derived from a host are well-known to those of skill in the art. Such assay methods include radio-immunoassays, competitive-binding assays, Western Blot analysis and ELISA assays.

Thus in another aspect, the present invention relates to a diagnostic kit comprising:

(a) a polynucleotide of the present invention, preferably the nucleotide sequence set forth in the Sequence Listing , or a fragment or an RNA transcript thereof;

(b) a nucleotide sequence complementary to that of (a);

(c) a polypeptide of the present invention, preferably the polypeptide set forth in the Sequence Listing or a fragment thereof; or

(d) an antibody to a polypeptide of the present invention, preferably to the polypeptide set forth in the Sequence Listing .

It will be appreciated that in any such kit, (a), (b), (c) or (d) may comprise a substantial component. Such a kit will be of use in diagnosing a disease or susceptibility to a disease, particularly diseases of the invention, amongst others.

The polynucleotide sequences of the present invention are valuable for chromosome localisation studies. The sequences set forth in the Sequence Listing are specifically targeted to, and can hybridize with, a particular location on an individual human chromosome. The mapping of relevant sequences to chromosomes according to the present invention is an important first step in correlating those sequences with gene associated disease. Once a sequence has been mapped to a precise chromosomal location, the physical position of the sequence on the chromosome can be correlated with genetic map data. Such data are found in, for example, V. McKusick, Mendelian Inheritance in Man (available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and diseases that have been mapped to the same chromosomal region are then identified through linkage analysis (co-inheritance of physically adjacent genes). Precise human chromosomal localisations for a genomic sequence (gene fragment etc.) can be determined using Radiation Hybrid (RH) Mapping (Walter, M. Spillett, D., Thomas, P., Weissenbach, J., and Goodfellow, P., (1994) A method for constructing radiation hybrid maps of whole genomes, Nature Genetics 7, 22-28). A number of RH panels are available from Research Genetics (Huntsville, AL, USA) e.g. the GeneBridge4 RH panel (Hum Mol Genet 1996 Mar;5(3):339-46 A radiation hybrid map of the human genome. Gyapay G, Schmitt K, Fizames C, Jones H, Vega-Czarny N, Spillett D, Muselet D, Prud'Homme JF, Dib C, Auffray C, Morissette J, Weissenbach J, Goodfellow PN). To determine the chromosomal location of a gene using this panel, 93 PCRs are performed using primers designed from the gene of interest on RH DNAs. Each of these DNAs contains random human genomic fragments maintained in a hamster background (human / hamster hybrid cell lines). These PCRs result in 93 scores indicating the presence or absence of the PCR product of the gene of interest. These scores are compared with scores created using PCR products from genomic sequences of known location. This comparison is conducted at http://www.genome.wi.mit.edu/.

The polynucleotide sequences of the present invention are also valuable tools for tissue expression studies. Such studies allow the determination of expression patterns of polynucleotides of the present invention which may give an indication as to the expression patterns of the encoded polypeptides in tissues, by detecting the mRNAs that encode them. The techniques used are well known in the art and include in situ hydridization techniques to clones arrayed on a grid, such as cDNA microarray hybridization (Schena *et al*, Science,

270, 467-470, 1995 and Shalon *et al*, Genome Res, 6, 639-645, 1996) and nucleotide amplification techniques such as PCR. A preferred method uses the TAQMAN (Trade mark) technology available from Perkin Elmer. Results from these studies can provide an indication of the normal function of the polypeptide in the organism. In addition, comparative studies of the normal expression pattern of mRNAs with that of mRNAs encoded by an alternative form of the same gene (for example, one having an alteration in polypeptide coding potential or a regulatory mutation) can provide valuable insights into the role of the polypeptides of the present invention, or that of inappropriate expression thereof in disease. Such inappropriate expression may be of a temporal, spatial or simply quantitative nature.

A further aspect of the present invention relates to antibodies. The polypeptides of the invention or their fragments, or cells expressing them, can be used as immunogens to produce antibodies that are immunospecific for polypeptides of the present invention. The term "immunospecific" means that the antibodies have substantially greater affinity for the polypeptides of the invention than their affinity for other related polypeptides in the prior art.

Antibodies generated against polypeptides of the present invention may be obtained by administering the polypeptides or epitope-bearing fragments, or cells to an animal, preferably a non-human animal, using routine protocols. For preparation of monoclonal antibodies, any technique which provides antibodies produced by continuous cell line cultures can be used. Examples include the hybridoma technique (Kohler, G. and Milstein, C., Nature (1975) 256:495-497), the trioma technique, the human B-cell hybridoma technique (Kozbor *et al.*, Immunology Today (1983) 4:72) and the EBV-hybridoma technique (Cole *et al.*, Monoclonal Antibodies and Cancer Therapy, 77-96, Alan R. Liss, Inc., 1985).

Techniques for the production of single chain antibodies, such as those described in U.S. Patent No. 4,946,778, can also be adapted to produce single chain antibodies to polypeptides of this invention. Also, transgenic mice, or other organisms, including other mammals, may be used to express humanized antibodies.

The above-described antibodies may be employed to isolate or to identify clones expressing the polypeptide or to purify the polypeptides by affinity chromatography. Antibodies against polypeptides of the present invention may also be employed to treat diseases of the invention, amongst others.

Polypeptides and polynucleotides of the present invention may also be used as vaccines. Accordingly, in a further aspect, the present invention relates to a method for

inducing an immunological response in a mammal that comprises inoculating the mammal with a polypeptide of the present invention, adequate to produce antibody and/or T cell immune response, including, for example, cytokine-producing T cells or cytotoxic T cells, to protect said animal from disease, whether that disease is already established within the individual or not. An immunological response in a mammal may also be induced by a method comprises delivering a polypeptide of the present invention *via* a vector directing expression of the polynucleotide and coding for the polypeptide *in vivo* in order to induce such an immunological response to produce antibody to protect said animal from diseases of the invention. One way of administering the vector is by accelerating it into the desired cells as a coating on particles or otherwise. Such nucleic acid vector may comprise DNA, RNA, a modified nucleic acid, or a DNA/RNA hybrid. For use a vaccine, a polypeptide or a nucleic acid vector will be normally provided as a vaccine formulation (composition). The formulation may further comprise a suitable carrier. Since a polypeptide may be broken down in the stomach, it is preferably administered parenterally (for instance, subcutaneous, intra-muscular, intravenous, or intra-dermal injection). Formulations suitable for parenteral administration include aqueous and non-aqueous sterile injection solutions that may contain anti-oxidants, buffers, bacteriostats and solutes that render the formulation instonic with the blood of the recipient; and aqueous and non-aqueous sterile suspensions that may include suspending agents or thickening agents. The formulations may be presented in unit-dose or multi-dose containers, for example, sealed ampoules and vials and may be stored in a freeze-dried condition requiring only the addition of the sterile liquid carrier immediately prior to use. The vaccine formulation may also include adjuvant systems for enhancing the immunogenicity of the formulation, such as oil-in water systems and other systems known in the art. The dosage will depend on the specific activity of the vaccine and can be readily determined by routine experimentation.

Polypeptides of the present invention have one or more biological functions that are of relevance in one or more disease states, in particular the diseases of the invention hereinbefore mentioned. It is therefore useful to identify compounds that stimulate or inhibit the function or level of the polypeptide. Accordingly, in a further aspect, the present invention provides for a method of screening compounds to identify those that stimulate or inhibit the function or level of the polypeptide. Such methods identify agonists or antagonists that may be employed for therapeutic and prophylactic purposes for such diseases of the invention as hereinbefore mentioned. Compounds may be identified from a variety of sources, for example, cells, cell-free preparations, chemical libraries, collections of chemical compounds, and natural product mixtures. Such agonists or antagonists so-

identified may be natural or modified substrates, ligands, receptors, enzymes, etc., as the case may be, of the polypeptide; a structural or functional mimetic thereof (see Coligan *et al.*, Current Protocols in Immunology 1(2):Chapter 5 (1991)) or a small molecule. Such small molecules preferably have a molecular weight below 2,000 daltons, more preferably between 300 and 1,000 daltons, and most preferably between 400 and 700 daltons. It is preferred that these small molecules are organic molecules.

The screening method may simply measure the binding of a candidate compound to the polypeptide, or to cells or membranes bearing the polypeptide, or a fusion protein thereof, by means of a label directly or indirectly associated with the candidate compound. Alternatively, the screening method may involve measuring or detecting (qualitatively or quantitatively) the competitive binding of a candidate compound to the polypeptide against a labeled competitor (*e.g.* agonist or antagonist). Further, these screening methods may test whether the candidate compound results in a signal generated by activation or inhibition of the polypeptide, using detection systems appropriate to the cells bearing the polypeptide. Inhibitors of activation are generally assayed in the presence of a known agonist and the effect on activation by the agonist by the presence of the candidate compound is observed. Further, the screening methods may simply comprise the steps of mixing a candidate compound with a solution containing a polypeptide of the present invention, to form a mixture, measuring an activity of the genes set forth in Table I in the mixture, and comparing activity of the mixture of the genes set forth in Table I to a control mixture which contains no candidate compound.

Polypeptides of the present invention may be employed in conventional low capacity screening methods and also in high-throughput screening (HTS) formats. Such HTS formats include not only the well-established use of 96- and, more recently, 384-well micotiter plates but also emerging methods such as the nanowell method described by Schullek et al, Anal Biochem., 246, 20-29, (1997).

Fusion proteins, such as those made from Fc portion and polypeptide of the genes set forth in Table I, as hereinbefore described, can also be used for high-throughput screening assays to identify antagonists for the polypeptide of the present invention (see D. Bennett *et al.*, J Mol Recognition, 8:52-58 (1995); and K. Johanson *et al.*, J Biol Chem, 270(16):9459-9471 (1995)).

The polynucleotides, polypeptides and antibodies to the polypeptide of the present invention may also be used to configure screening methods for detecting the effect of added compounds on the production of mRNA and polypeptide in cells. For example, an ELISA assay may be constructed for measuring secreted or cell associated levels of polypeptide

using monoclonal and polyclonal antibodies by standard methods known in the art. This can be used to discover agents that may inhibit or enhance the production of polypeptide (also called antagonist or agonist, respectively) from suitably manipulated cells or tissues.

A polypeptide of the present invention may be used to identify membrane bound or soluble receptors, if any, through standard receptor binding techniques known in the art. These include, but are not limited to, ligand binding and crosslinking assays in which the polypeptide is labeled with a radioactive isotope (for instance, ^{125}I), chemically modified (for instance, biotinylated), or fused to a peptide sequence suitable for detection or purification, and incubated with a source of the putative receptor (cells, cell membranes, cell supernatants, tissue extracts, bodily fluids). Other methods include biophysical techniques such as surface plasmon resonance and spectroscopy. These screening methods may also be used to identify agonists and antagonists of the polypeptide that compete with the binding of the polypeptide to its receptors, if any. Standard methods for conducting such assays are well understood in the art.

Examples of antagonists of polypeptides of the present invention include antibodies or, in some cases, oligonucleotides or proteins that are closely related to the ligands, substrates, receptors, enzymes, etc., as the case may be, of the polypeptide, *e.g.*, a fragment of the ligands, substrates, receptors, enzymes, etc.; or a small molecule that bind to the polypeptide of the present invention but do not elicit a response, so that the activity of the polypeptide is prevented.

Screening methods may also involve the use of transgenic technology and the genes set forth in Table I. The art of constructing transgenic animals is well established. For example, the genes set forth in Table I may be introduced through microinjection into the male pronucleus of fertilized oocytes, retroviral transfer into pre- or post-implantation embryos, or injection of genetically modified, such as by electroporation, embryonic stem cells into host blastocysts. Particularly useful transgenic animals are so-called "knock-in" animals in which an animal gene is replaced by the human equivalent within the genome of that animal. Knock-in transgenic animals are useful in the drug discovery process, for target validation, where the compound is specific for the human target. Other useful transgenic animals are so-called "knock-out" animals in which the expression of the animal ortholog of a polypeptide of the present invention and encoded by an endogenous DNA sequence in a cell is partially or completely annulled. The gene knock-out may be targeted to specific cells or tissues, may occur only in certain cells or tissues as a consequence of the limitations of the technology, or may occur in all, or substantially all, cells in the animal. Transgenic animal technology also offers a whole animal expression-cloning system in which

introduced genes are expressed to give large amounts of polypeptides of the present invention

Screening kits for use in the above described methods form a further aspect of the present invention. Such screening kits comprise:

(a) a polypeptide of the present invention;

(b) a recombinant cell expressing a polypeptide of the present invention;

(c) a cell membrane expressing a polypeptide of the present invention; or

(d) an antibody to a polypeptide of the present invention;

which polypeptide is preferably that set forth in the Sequence Listing.

It will be appreciated that in any such kit, (a), (b), (c) or (d) may comprise a substantial component.

Glossary

The following definitions are provided to facilitate understanding of certain terms used frequently hereinbefore.

"Antibodies" as used herein includes polyclonal and monoclonal antibodies, chimeric, single chain, and humanized antibodies, as well as Fab fragments, including the products of an

Fab or other immunoglobulin expression library.

"Isolated" means altered "by the hand of man" from its natural state, *i.e.*, if it occurs in nature, it has been changed or removed from its original environment, or both. For example, a polynucleotide or a polypeptide naturally present in a living organism is not "isolated," but the same polynucleotide or polypeptide separated from the coexisting materials of its natural state is "isolated", as the term is employed herein. Moreover, a polynucleotide or polypeptide that is introduced into an organism by transformation, genetic manipulation or by any other recombinant method is "isolated" even if it is still present in said organism, which organism may be living or non-living.

"Secreted protein activity or secreted polypeptide activity" or "biological activity of the secreted protein or secreted polypeptide" refers to the metabolic or physiologic function of said secreted protein including similar activities or improved activities or these activities with decreased undesirable side-effects. Also included are antigenic and immunogenic activities of said secreted protein.

"Secreted protein gene" refers to a polynucleotide comprising any of the attached nucleotide sequences or allelic variants thereof and/or their complements.

"Polynucleotide" generally refers to any polyribonucleotide (RNA) or polydeoxribonucleotide (DNA), which may be unmodified or modified RNA or DNA. "Polynucleotides" include, without limitation, single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, "polynucleotide" refers to triple-stranded regions comprising RNA or DNA or both RNA and DNA. The term "polynucleotide" also includes DNAs or RNAs containing one or more modified bases and DNAs or RNAs with backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications may be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically or metabolically modified forms of polynucleotides as typically found in nature, as well as the chemical forms of DNA and RNA characteristic of viruses and cells. "Polynucleotide" also embraces relatively short polynucleotides, often referred to as oligonucleotides.

"Polypeptide" refers to any polypeptide comprising two or more amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres. "Polypeptide" refers to both short chains, commonly referred to as peptides, oligopeptides or oligomers, and to longer chains, generally referred to as proteins. Polypeptides may contain amino acids other than the 20 gene-encoded amino acids. "Polypeptides" include amino acid sequences modified either by natural processes, such as post-translational processing, or by chemical modification techniques that are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous research literature. Modifications may occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present to the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched and branched cyclic polypeptides may result from post-translation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, biotinylation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphotidylinositol, cross-

linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cystine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination (see, for instance, Proteins - Structure and Molecular Properties, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York, 1993; Wold, F., Post-translational Protein Modifications: Perspectives and Prospects, 1-12, in Post-translational Covalent Modification of Proteins, B. C. Johnson, Ed., Academic Press, New York, 1983; Seifter *et al.*, "Analysis for protein modifications and nonprotein cofactors", Meth Enzymol, 182, 626-646, 1990, and Rattan *et al.*, "Protein Synthesis: Post-translational Modifications and Aging", Ann NY Acad Sci, 663, 48-62, 1992).

"Fragment" of a polypeptide sequence refers to a polypeptide sequence that is shorter than the reference sequence but that retains essentially the same biological function or activity as the reference polypeptide. "Fragment" of a polynucleotide sequence refers to a polynucleotide sequence that is shorter than the reference sequence set forth in the Sequence Listing.

"Variant" refers to a polynucleotide or polypeptide that differs from a reference polynucleotide or polypeptide, but retains the essential properties thereof. A typical variant of a polynucleotide differs in nucleotide sequence from the reference polynucleotide. Changes in the nucleotide sequence of the variant may or may not alter the amino acid sequence of a polypeptide encoded by the reference polynucleotide. Nucleotide changes may result in amino acid substitutions, additions, deletions, fusions and truncations in the polypeptide encoded by the reference sequence, as discussed below. A typical variant of a polypeptide differs in amino acid sequence from the reference polypeptide. Generally, alterations are limited so that the sequences of the reference polypeptide and the variant are closely similar overall and, in many regions, identical. A variant and reference polypeptide may differ in amino acid sequence by one or more substitutions, insertions, deletions in any combination. A substituted or inserted amino acid residue may or may not be one encoded by the genetic code. Typical conservative substitutions include Gly, Ala; Val, Ile, Leu; Asp, Glu; Asn, Gln; Ser, Thr; Lys, Arg; and Phe and Tyr. A variant of a polynucleotide or polypeptide may be naturally occurring such as an allele, or it may be a variant that is not known to occur naturally. Non-naturally occurring variants of polynucleotides and polypeptides may be made by mutagenesis techniques or by direct synthesis. Also included as variants are polypeptides having one or more post-translational modifications, for

instance glycosylation, phosphorylation, methylation, ADP ribosylation and the like. Embodiments include methylation of the N-terminal amino acid, phosphorylations of serines and threonines and modification of C-terminal glycines.

"Allele" refers to one of two or more alternative forms of a gene occurring at a given locus in the genome.

"Polymorphism" refers to a variation in nucleotide sequence (and encoded polypeptide sequence, if relevant) at a given position in the genome within a population.

"Single Nucleotide Polymorphism" (SNP) refers to the occurrence of nucleotide variability at a single nucleotide position in the genome, within a population. An SNP may occur within a gene or within intergenic regions of the genome. SNPs can be assayed using Allele Specific Amplification (ASA). For the process at least 3 primers are required. A common primer is used in reverse complement to the polymorphism being assayed. This common primer can be between 50 and 1500 bps from the polymorphic base. The other two (or more) primers are identical to each other except that the final 3' base wobbles to match one of the two (or more) alleles that make up the polymorphism. Two (or more) PCR reactions are then conducted on sample DNA, each using the common primer and one of the Allele Specific Primers.

"Splice Variant" as used herein refers to cDNA molecules produced from RNA molecules initially transcribed from the same genomic DNA sequence but which have undergone alternative RNA splicing. Alternative RNA splicing occurs when a primary RNA transcript undergoes splicing, generally for the removal of introns, which results in the production of more than one mRNA molecule each of that may encode different amino acid sequences. The term splice variant also refers to the proteins encoded by the above cDNA molecules.

"Identity" reflects a relationship between two or more polypeptide sequences or two or more polynucleotide sequences, determined by comparing the sequences. In general, identity refers to an exact nucleotide to nucleotide or amino acid to amino acid correspondence of the two polynucleotide or two polypeptide sequences, respectively, over the length of the sequences being compared.

"% Identity" - For sequences where there is not an exact correspondence, a "% identity" may be determined. In general, the two sequences to be compared are aligned to give a maximum correlation between the sequences. This may include inserting "gaps" in either one or both sequences, to enhance the degree of alignment. A % identity may be determined over the whole length of each of the sequences being compared (so-called global alignment), that is particularly suitable for sequences of the same or very similar length, or

over shorter, defined lengths (so-called local alignment), that is more suitable for sequences of unequal length.

"Similarity" is a further, more sophisticated measure of the relationship between two polypeptide sequences. In general, "similarity" means a comparison between the amino acids of two polypeptide chains, on a residue by residue basis, taking into account not only exact correspondences between a between pairs of residues, one from each of the sequences being compared (as for identity) but also, where there is not an exact correspondence, whether, on an evolutionary basis, one residue is a likely substitute for the other. This likelihood has an associated "score" from which the "% similarity" of the two sequences can then be determined.

Methods for comparing the identity and similarity of two or more sequences are well known in the art. Thus for instance, programs available in the Wisconsin Sequence Analysis Package, version 9.1 (Devereux J et al, Nucleic Acids Res, 12, 387-395, 1984, available from Genetics Computer Group, Madison, Wisconsin, USA), for example the programs BESTFIT and GAP, may be used to determine the % identity between two polynucleotides and the % identity and the % similarity between two polypeptide sequences. BESTFIT uses the "local homology" algorithm of Smith and Waterman (J Mol Biol, 147,195-197, 1981, Advances in Applied Mathematics, 2, 482-489, 1981) and finds the best single region of similarity between two sequences. BESTFIT is more suited to comparing two polynucleotide or two polypeptide sequences that are dissimilar in length, the program assuming that the shorter sequence represents a portion of the longer. In comparison, GAP aligns two sequences, finding a "maximum similarity", according to the algorithm of Neddleman and Wunsch (J Mol Biol, 48, 443-453, 1970). GAP is more suited to comparing sequences that are approximately the same length and an alignment is expected over the entire length. Preferably, the parameters "Gap Weight" and "Length Weight" used in each program are 50 and 3, for polynucleotide sequences and 12 and 4 for polypeptide sequences, respectively. Preferably, % identities and similarities are determined when the two sequences being compared are optimally aligned.

Other programs for determining identity and/or similarity between sequences are also known in the art, for instance the BLAST family of programs (Altschul S F et al, J Mol Biol, 215, 403-410, 1990, Altschul S F et al, Nucleic Acids Res., 25:389-3402, 1997, available from the National Center for Biotechnology Information (NCBI), Bethesda, Maryland, USA and accessible through the home page of the NCBI at www.ncbi.nlm.nih.gov) and FASTA (Pearson W R, Methods in Enzymology, 183, 63-99,

1990; Pearson W R and Lipman D J, Proc Nat Acad Sci USA, 85, 2444-2448,1988, available as part of the Wisconsin Sequence Analysis Package).

Preferably, the BLOSUM62 amino acid substitution matrix (Henikoff S and Henikoff J G, Proc. Nat. Acad Sci. USA, 89, 10915-10919, 1992) is used in polypeptide sequence comparisons including where nucleotide sequences are first translated into amino acid sequences before comparison.

Preferably, the program BESTFIT is used to determine the % identity of a query polynucleotide or a polypeptide sequence with respect to a reference polynucleotide or a polypeptide sequence, the query and the reference sequence being optimally aligned and the parameters of the program set at the default value, as hereinbefore described.

"Identity Index" is a measure of sequence relatedness which may be used to compare a candidate sequence (polynucleotide or polypeptide) and a reference sequence. Thus, for instance, a candidate polynucleotide sequence having, for example, an Identity Index of 0.95 compared to a reference polynucleotide sequence is identical to the reference sequence except that the candidate polynucleotide sequence may include on average up to five differences per each 100 nucleotides of the reference sequence. Such differences are selected from the group consisting of at least one nucleotide deletion, substitution, including transition and transversion, or insertion. These differences may occur at the 5' or 3' terminal positions of the reference polynucleotide sequence or anywhere between these terminal positions, interspersed either individually among the nucleotides in the reference sequence or in one or more contiguous groups within the reference sequence. In other words, to obtain a polynucleotide sequence having an Identity Index of 0.95 compared to a reference polynucleotide sequence, an average of up to 5 in every 100 of the nucleotides of the in the reference sequence may be deleted, substituted or inserted, or any combination thereof, as hereinbefore described. The same applies *mutatis mutandis* for other values of the Identity Index, for instance 0.96, 0.97, 0.98 and 0.99.

Similarly, for a polypeptide, a candidate polypeptide sequence having, for example, an Identity Index of 0.95 compared to a reference polypeptide sequence is identical to the reference sequence except that the polypeptide sequence may include an average of up to five differences per each 100 amino acids of the reference sequence. Such differences are selected from the group consisting of at least one amino acid deletion, substitution, including conservative and non-conservative substitution, or insertion. These differences may occur at the amino- or carboxy-terminal positions of the reference polypeptide sequence or anywhere between these terminal positions, interspersed either individually among the amino acids in the reference sequence or in one or more contiguous groups

within the reference sequence. In other words, to obtain a polypeptide sequence having an Identity Index of 0.95 compared to a reference polypeptide sequence, an average of up to 5 in every 100 of the amino acids in the reference sequence may be deleted, substituted or inserted, or any combination thereof, as hereinbefore described. The same applies *mutatis mutandis* for other values of the Identity Index, for instance 0.96, 0.97, 0.98 and 0.99.

The relationship between the number of nucleotide or amino acid differences and the Identity Index may be expressed in the following equation:

$$n_a \leq x_a - (x_a \bullet I),$$

in which:

n_a is the number of nucleotide or amino acid differences,

x_a is the total number of nucleotides or amino acids in a sequence set forth in the Sequence Listing,

I is the Identity Index,

• is the symbol for the multiplication operator, and

in which any non-integer product of x_a and I is rounded down to the nearest integer prior to subtracting it from x_a.

"Homolog" is a generic term used in the art to indicate a polynucleotide or polypeptide sequence possessing a high degree of sequence relatedness to a reference sequence. Such relatedness may be quantified by determining the degree of identity and/or similarity between the two sequences as hereinbefore defined. Falling within this generic term are the terms "ortholog", and "paralog". "Ortholog" refers to a polynucleotide or polypeptide that is the functional equivalent of the polynucleotide or polypeptide in another species. "Paralog" refers to a polynucleotideor polypeptide that within the same species which is functionally similar.

"Fusion protein" refers to a protein encoded by two, often unrelated, fused genes or fragments thereof. In one example, EP-A-0 464 533-A discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, employing an immunoglobulin Fc region as a part of a fusion protein is advantageous for use in therapy and diagnosis resulting in, for example, improved pharmacokinetic properties [see, *e.g.*, EP-A 0232 262]. On the other hand, for some uses it would be desirable to be able to delete the Fc part after the fusion protein has been expressed, detected and purified.

All publications and references, including but not limited to patents and patent applications, cited in this specification are herein incorporated by reference in their entirety as if each individual publication or reference were specifically and individually indicated to

be incorporated by reference herein as being fully set forth. Any patent application to which this application claims priority is also incorporated by reference herein in its entirety in the manner described above for publications and references.

Table I.

Gene Name	GSK Gene ID	Nucleic Acid SEQ ID NO's	Corresponding Protein SEQ ID NO's
sbg318680DNase	318680	SEQ ID NO:1	SEQ ID NO:40
sbg237038SA	237038	SEQ ID NO:2 SEQ ID NO:3	SEQ ID NO:41 SEQ ID NO:42
sbg340871GPV	340871	SEQ ID NO:4	SEQ ID NO:43
sbg293416HNKS	293416	SEQ ID NO:5 SEQ ID NO:6	SEQ ID NO:44 SEQ ID NO:45
sbg257418ZP	257418	SEQ ID NO:7	SEQ ID NO:46
sbg319185CDa	319185	SEQ ID NO:8 SEQ ID NO:9	SEQ ID NO:47 SEQ ID NO:48
sbg323307KIAAa	323307	SEQ ID NO:10	SEQ ID NO:49
sbg315953GPPa	315953	SEQ ID NO:11 SEQ ID NO:12	SEQ ID NO:50 SEQ ID NO:51
sbg318486ONC	318486	SEQ ID NO:13	SEQ ID NO:52
sbg299359LIPO	299359	SEQ ID NO:14	SEQ ID NO:53
sbg230022NGa	230022	SEQ ID NO:15 SEQ ID NO:16	SEQ ID NO:54 SEQ ID NO:55
sbg297169BGP	297169	SEQ ID NO:17 SEQ ID NO:18	SEQ ID NO:56 SEQ ID NO:57
sbg253919HSCCAa	253919	SEQ ID NO:19 SEQ ID NO:20	SEQ ID NO:58 SEQ ID NO:59
sbg228137OLF	228137	SEQ ID NO:21 SEQ ID NO:22	SEQ ID NO:60 SEQ ID NO:61
sbg378514Netrin	378514	SEQ ID NO:23 SEQ ID NO:24	SEQ ID NO:62 SEQ ID NO:63
sbg253227.mucous matrix glycoprotein	253227	SEQ ID NO:25 SEQ ID NO:26	SEQ ID NO:64 SEQ ID NO:65
sbg262831SIAa	262831	SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:66 SEQ ID NO:67
sbg233728LIPASE	233728	SEQ ID NO:29	SEQ ID NO:68
sbg400455.CRF	400455	SEQ ID NO:30	SEQ ID NO:69
sbg400612KINASEa	400612	SEQ ID NO:31	SEQ ID NO:70
sbg381373ACRP	381373	SEQ ID NO:32	SEQ ID NO:71
sbg401294MEX-3	401294	SEQ ID NO:33 SEQ ID NO:34	SEQ ID NO:72 SEQ ID NO:73
sbg247722Cadherin	247722	SEQ ID NO:35 SEQ ID NO:36	SEQ ID NO:74 SEQ ID NO:75
sbg391057THIPa	391057	SEQ ID NO:37 SEQ ID NO:38	SEQ ID NO:76 SEQ ID NO:77
sbg378067TGFc	378067	SEQ ID NO:39	SEQ ID NO:78

Table II

Gene Name	Gene Family	Closest Polynuclotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg318680-DNase	DNase I	GB:AC022471 Sbmitted (04-FEB-2000) by Lita Annenberg Hazen Genome Sequencing Center, Cold Spring Harbor Laboratory, 1 Bungtown Road, Cold Spring Harbor, NY 11724, USA.	Human DNase I-like endonuclease, gi:5803007 Parrish JE, Ciccodicola A, Wehhert M, Cox GF, Chen E, and Nelson DL; 1995; Hum. Mol. Genet. 4:1557-1564.	Secreted
sbg237038-SA	SA protein	GB:AC023292 Submitted (11-FEB-2000) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA.	Human SA gene, gi:2988399 Loftus,B.J. et al. Genomics 60 (3), 295-308 (1999)	Secreted
sbg340871-GPV	Platelet glycoprotein (GPV)	GB:AC025389 Submitted (08-MAR-2000) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA.	Rat platelet glycoprotein V (GPV) precursor, gi:6980974 Ravanat C, Morales M, Azorsa DO, Moog S, Schuhler S, Grunert P, Loew D, Van Dorsselaer A, Cazenave JP, Lanza F; 1997; Blood 89:3253-62.	Secreted
sbg293416-HNKS	HNK-1 sulfotransferase	JGI:LLNL-R_241B6 Joint Genome Institute, Department of Energy, USA	Human GalNAc 4-sulfotransferase, gi:11990885 Okuda,T., Mita,S., Yamauchi,S., Fukuta,M., Nakano,H., Sawada,T. and Habuchi,O. J. Biol. Chem. 275 (51), 40605-40613 (2000)	Secreted
sbg257418-ZP	Zona pellucida protein	GB:AP000777 Submitted (25-NOV-1999) to the DDBJ/EMBL/GenBank databases. Masahira Hattori, The Institute of Physical and Chemical Research (RIKEN), Genomic Sciences Center (GSC); Kitasato Univ., 1-15-1 Kitasato, Sagamihara, Kanagawa 228-8555, Japan.	Mouse zona pellucida glycoprotein, gi:6677653 Epifano,O., Liang,L.F., Familari,M., Moos,M.C. Jr. and Dean,J.; 1995; Development 121:1947-1956.	Secreted

Table II (cont).

Gene Name	Gene Family	Closest Polynuclotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg319185-CDa	Leukocyte differentiation antigen	GB:AC024004 Submitted (20-FEB-2000) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Human leukocyte differentiation antigen CD84 isoform CD84s, gi:6650112 Submitted (20-MAR-1998) by Servei d'Immunologia, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain	Secreted
sbg323307-KIAAa	Slit-like	GB:AL160156, Submitted (10-MAR-2000) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human unnamed protein, gi:10439289 Submitted (29-AUG-2000) by Sumio Sugano, Institute of Medical Science, University of Tokyo, Laboratory of Genome Structure Analysis, Human Genome Center; Shirokane-dai, 4-6-1, Minato-ku, Tokyo 108-8639, Japan	Secreted
sbg315953-GPPa	Granulocyte peptide A	GB:AC011666 Submitted (09-OCT-1999) by Department Of Chemistry And Biochemistry, The University Of Oklahoma, 620 Parrington Oval, Room 208, Norman, OK 73019, USA	Human hypothetical protein SBBI67, gi:9966869 Submitted (08-MAR-2000) by Department of Immunology, Second Military Medical University & Shanghai Brilliance Biotechnology Institute, 800 Xiangyin Rd., Shanghai 200433, P.R. China	Secreted
sbg318486-ONC	Oncotrophoblast glycoprotein	GB:AC022045 Submitted (25-JAN-2000) by tehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA.	Canine 5T4 tumour-associated antigen' geneseqp:Y94351 Submitted by OXFORD BIOMEDICA UK LTD Publication number and date: WO200029428-A2, 25-MAY-00	Secreted

Table II (cont).

Gene Name	Gene Family	Closest Polynuclotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg29935 9-LIPO	Lipocalin	SC:AL139041 Submitted (16-NOV-2000) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK	Mouse major urinary protein (MUP) 4, gi:6678968 Shahan K, Gilmartin M, and Derman E; 1987; Mol Cell Biol 7:1938-1946.	Secreted
sbg23002 2-NGa	Plasmacytoma -associated neuronal glycoprotein	GB:AC066608 GB:AC022002 Submitted (25-APR-2000) and (24-JAN-2000) by Human Genomic Center, Institute of Genetics, Chinese Academy of Sciences, Datun Road, Beijing, Beijing 100101, P.R.China	Rat neural cell adhesion protein BIG-2 precursor, gi :1016012 Yoshihara,Y., Kawasaki,M., Tamada,A., Nagata,S., Kagamiyama,H. and Mori,K. J. Neurobiol. 28 (1), 51-69 (1995)	Membrane-bound
sbg29716 9-BGP	Biliary glycoprotien (BGP)	JGI: CITB-E1_2616J11 Submitted by Joint Genome Institute, Department of Energy, USA	Mouse biliary glycoprotein (BGP), gi:312584 McCuaig K, Rosenberg M, Nedellec P, Turbide C, and Beauchemin N; 1993; Gene 127:173-83.	Secreted
sbg25391 9-HSCCAa	Human squamous cell carcinoma antigen (SCCA)	GB:AC019355 Submitted (02-JAN-2000) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Human squamous cell carcinoma antigen 2 (SCCA-2) (LEUPIN). gi:1710877. Schneider,S.S., Schick,C., Fish,K.E., Miller,E., Pena,J.C., Treter,S.D., Hui,S.M. and Silverman,G.A. Proc. Natl. Acad. Sci. U.S.A. 92 (8), 3147-3151 (1995).	Secreted
sbg22813 7-OLF	Olfactomedin -related protein	GB:AC022606 Submitted (06-FEB-2000) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Rat neuronal olfactomedin-related protein precursor, gi:3024210 Danielson,P.E., Forss-Petter,S., Battenberg,E.L., deLecea,L., Bloom,F.E., and Sutcliffe,J.G., 1994, J. Neurosci. Res. 38:468-478.	Secreted

Table II (cont).

Gene Name	Gene Family	Closest Polynuclotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg378514-Netrin	Netrin precursor	SC:BA5N16 Submitted (09-APR-2001) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Mouse Netrin-G1a protein gi:9909148 Nakashiba,T., Ikeda,T., Nishimura,S., Tashiro,K., Honjo,T., Culotti,J.G. and Itohara,S. J. Neurosci. 20 (17), 6540-6550 (2000)	Secreted
sbg253227. mucous matrix glycoprotei n	Extracellular mucous matrix glycoprotein (EMMG)	GB:AC011647 Submitted (08-OCT-1999) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Human colon specific protein, geneseqp:Y54368 Submitted by DIADEXUS LLC Publication number and date: WO9960161-A1, 25-NOV-99	Secreted
sbg262831-SIAa	Sialoadhesin	JGI:CITB-E1_3073N11 Found at Joint Genome Institute	Human sialic acid binding immunoglobulin-like lectin 8 long splice variant, gi: 9837433 Foussias,G., Yousef,G.M. and Diamandis,E.P. Biochem. Biophys. Res. Commun. 278 (3), 775-781 (2000)	Secreted
sbg233728-LIPASE	Pancreatic lipase	GB:AC011098 Submitted (01-OCT-1999) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA.	Human pancreatic lipase precursor, gi:126318 Lowe ME, Rosenblum JL, and Strauss AW; 1989; J Biol Chem 264:20042-8.	Secreted
sbg400455. -CRF	C1q-related factor (CRF)	GB:AC024339 Submitted (28-FEB-2000) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	MouseGliacolin, gi:10566471 Koide,T., Aso,A., Yorihuzi,T. and Nagata,K. J. Biol. Chem. 275 (36), 27957-27963 (2000)	Secreted

Table II (cont).

Gene Name	Gene Family	Closest Polynuclotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg400612-KINASEa	Protein kinase	GB:AP001615 Submitted (04-APR-2000) to the DDBJ/EMBL/GenBank databases. Nobuyoshi Shimizu, Keio University, School of Medicine, Molecular Biology; 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan	Murine protein kinase/ankyrin homologue, geneseqp:Y76079 Submitted by GENESIS RES & DEV CORP LTD Publication number and date: WO9955865-A1 04-NOV-99	Secreted
sbg381373-ACRP	Adipocyte complement -related protein (ACRP30)	JGI:RPCI-11_161M6 Found at Joint Genome Institute, Department of Energy, USA	Human adipocyte Complement-Related Protein (ACRP30R2), geneseqp:Y44487. Submitted by SMITHKLINE BEECHAM CORP Publication number and date: WO9964629-A1, 16-DEC-99	Secreted
sbg401294-MEX-3	MEX-3(IAP)	GB:AC026956 Submitted (25-MAR-2000) by Whitehead Institute/ MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Caenorhabditis elegans MEX-3, gi:1644450 Draper,B.W., Mello,C.C., Bowerman,B., Hardin,J. and Priess,J.R. Cell 87 (2), 205-216 (1996)	Cyto solic (RNA-binding protein)
sbg247722-Cadherin	OB-Cadherin	GB:AL132780 Submitted (02-NOV-1999) by Genoscope - Centre National de Sequencage : BP 191 91006 EVRY cedex - FRANCE	Human OB-cadherin-1, gi:1377894 Okazaki,M., Takeshita,S., Kawai,S., Kikuno,R., Tsujimura,A., Kudo,A. and Amann,E. J. Biol. Chem. 269 (16), 12092-12098 (1994)	Secreted

Table II (cont).

Gene Name	Gene Family	Closest Polynuclotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg391057-THIPa	Thyroid hormone induced protein	SC:AL158153, SC:AL392044 Submitted (22-MAR-2001) and (02-MAR-2001) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human TANGO 239, geneseqp:B01432 Submitted by MILLENNIUM PHARM INC Publication number and date: WO200039284-A1, 06-JUL-00	Secreted
sbg378067-TGFc	TGF beta (transforming growth factor beta)	SC:AL162502 Submitted (06-APR-2001) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human persephin growth factor, geneseqp:Y16714 Submitted by UNIV WASHINGTON Publication number and date: WO9914235-A1 25-MAR-99	Secreted

Table III.

Gene Name	Uses	Associated Diseases
sbg318680-DNase	An embodiment of the invention is the use of sbg318680-Dnase to treat respiratory diseases and target parasites or cancer cells as a chromosome degrading agent to cause death of those cells. Close homologues of sbg318680-DNase are DNases. DNase can be used to treat respiratory diseases, such as pneumonia, cystic fibrosis and asthma, by reducing viscosity of bronchopulmonary secretions (MacConnachie AM; 1999; Intensive Crit Care Nurs 14:101-2).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation and respiratory diseases
sbg237038-SA	An embodiment of the invention is the use of sbg237038SA in blood pressure control. A close homologue of sbg237038SA is the rat SA gene. The SA gene is expressed at higher levels in the kidney of genetically hypertensive rats (Yang T, Hassan SA, Singh I, Smart A, Brosius FC, Holzman LB, Schnermann JB, Briggs JP; 1996; Hypertension 27:541-51).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, and hypertension
sbg340871-GPV	An embodiment of the invention is the use of sbg340871-GPV in hemostasis and platelet aggregation. A close homologue of sbg340871-GPV is platelet glycoprotein (GP) V. Platelet glycoprotein (GP) V is a major surface protein which is cleaved by thrombin during platelet activation, and associates with GPIb-IX complex to form GPIb-V-IX, a receptor for von Willebrand factor and thrombin. Its functional role in hemostasis is possibly related to thrombin-induced platelet aggregation (Ravanat C, Morales M, Azorsa DO, Moog S, Schuhler S, Grunert P, Loew D, Van Dorsselaer A, Cazenave JP, Lanza F; 1997; Blood 89:3253-62).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, and Bernard-Soulier disease
sbg293416-HNKS	An embodiment of the invention is the use of sbg293416-HNKS in cell interactions and the development of the nervous system. Close homologues of sbg293416-HNKS are sulfotransferases. Sulfotransferases are considered to be key enzymes in the biosynthesis of the HNK-1 carbohydrate epitope, which is expressed on several neural adhesion glycoproteins and as a glycolipid, and is involved in cell interactions (Bakker,H., Friedmann,I., Oka,S., Kawasaki,T., Nifant'ev,N., Schachner,M. and Mantei,N., 1997, J. Biol. Chem. 272:29942-29946). The HNK-1 epitope is spatially and temporally regulated during the development of the nervous system. The biological function of the HNK-1 sulfotransferase may be related to the development of the nervous system, and also may be involved in the preferential reinervation of muscle nerves by motor axons after lesion (Jungalwala FB, 1994, Neurochem Res 19:945-57).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, and peripheral neuropathies

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg257418-ZP	An embodiment of the invention is the use of sbg257418ZP in fertilization. A close homologue of sbg257418ZP is zona pellucida. Zona pellucida protein is an extracellular matrix that surrounds growing oocytes, ovulated eggs, and early embryos and it is critically involved in fertilization (Epifano,O., Liang,L.F., Familari,M., Moos,M.C. Jr. and Dean,J.; 1995; Development 121:1947-1956). The zona pellucida also provides a post-fertilization block to polyspermy and protects the growing embryo as it passes down the oviduct (Rankin T, and Dean J; 1996; Mol Hum Reprod 2:889-94).	Infertility
sbg319185-CDa	An embodiment of the invention is the use of sbg319185CDa, a secreted protein, in the diagnosis and treatment of cancer and autoimmune disorders. Close homologues of sbg319185CDa are leukocyte differentiation antigen CD84 isoforms. CD84's are members of the immunoglobulin superfamily, show high homology with several molecules belonging to the CD2 family of differentiation antigens and is proposed to be useful in the diagnosis and treatment of cancer and autoimmune disorders (Palou E, Pirotto F, Sole J, Freed JH, Peral B, Vilardell C, Vilella R, Vives J, Gaya A. Genomic characterization of CD84 reveals the existence of five isoforms differing in their cytoplasmic domains. Tissue Antigens 2000 Feb;55(2):118-27)).	Cancer, autoimmune disorders, wound healing disorders, infections and hematopoietic disorders
sbg323307-KIAAa	An embodiment of the invention is the use of sbg323307-KIAAa, a secreted protein, to regulate cell signaling, motility, and nucleic acid management. A close homologue of sbg323307-KIAAa is human KIAA0918 protein. Human KIAA0918 protein, a slit-like protein is functionally related to cell signaling/communication, cell structure/motility and nucleic acid management (Nagase,T., Ishikawa,K., Suyama,M., Kikuno,R., Hirosawa,M., Miyajima,N., Tanaka,A., Kotani,H., Nomura,N. and Ohara,O. KIAA0918 protein [Homo sapiens], DNA Res. 5 (6), 355-364 (1998)).	Cancer, autoimmune disorders, infections, wound healing disorders and hematopoietic disorders

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg315953-GPPa	An embodiment of the invention is the use of sbg315953GPPa, a secreted protein, to treat disorders associated with lipopolysaccharides. A close homologue to sbg315953GPPa is Bovine granulocyte peptide A precursor. Bovine granulocyte peptide A precursors are used in human and veterinary medicine, particularly to treat disorders associated with lipopolysaccharides, e.g. sepsis and endotoxaemia (1. Selsted ME, Bovine granulocyte peptide A precursor (antimicrobial BGP-A). Accession Number W23722, Publication Date 21-AUG-97. 2. Yount NY, Yuan J, Tarver A, Castro T, Diamond G, Tran PA, Levy JN, McCullough C, Cullor JS, Bevins CL, Selsted ME. Cloning and expression of bovine neutrophil beta-defensins. Biosynthetic profile during neutrophilic maturation and localization of mature peptide to novel cytoplasmic dense granules. J Biol Chem 1999 Sep 10;274(37):26249-58)).	Infections, cancer, autoimmune disorders, wounder healing disorders and hematopoietic disorders.
sbg318486-ONC	An embodiment of the invention is the use of sbg318486ONC in the growth and invasion events of trophoblast and tumor cells. A close homologue to sbg318486ONC is oncotrophoblast glycoproteins. It has been shown that oncotrophoblast protein was expressed by tumor cells with metastatic spread, suggesting a role in invasion during cancer (King,K.W., Sheppard,F.C., Westwater,C., Stern,P.L. and Myers,K.A.; 1999; Biochim. Biophys. Acta 1445, 257-270).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, and inflammation
sbg299359-LIPO	An embodiment of the invention is the use of sbg299359LIPO in sperm maturation, taste recognition, and transportation of some molecules across the blood brain barrier. A close homologue to sbg299359LIPO is Lipocalin. Lipocalins transport small hydrophobic molecules such as steroids, bilins, retinoids, and lipids, and they have various effects on a number of tissues. It has been shown that lipocalins are involved in sperm maturation, taste recognition, and transportation of some molecules across the blood brain barrier (Newcomer M.E.; 1993; Structure 1:7-18; Achen M.G., Harms P.J., Thomas T., Richardson S.J., Wettenhall R.E.H., Schreiber G.; 1992; J. Biol. Chem. 267:23170-23174)	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, and inflammation

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg230022-NGa	An embodiment of the invention is the use of sbg230022Nga in the formation and maintenance of neuron type-specific networks in the brain. Close homologues to sbg230022Nga are mouse plasmacytoma-associated neuronal glycoprotein and rat BIG-1 protein. Mouse plasmacytoma-associated neuronal glycoprotein, is ectopically activated by intracisternal A-type particle long terminal repeats in murine plasmacytomas. Rat BIG-1 protein, is a TAG-1/F3-related member of the immunoglobulin superfamily with neurite outgrowth-promoting activity and involved in the formation and maintenance of neuron type-specific networks in the brain (1. Connelly MA, Grady RC, Mushinski JF, Marcu KB. PANG, a gene encoding a neuronal glycoprotein, is ectopically activated by intracisternal A-type particle long terminal repeats in murine plasmacytomas. Proc Natl Acad Sci U S A 1994 Feb 15;91(4):1337-41 2. Yoshihara Y, Kawasaki M, Tani A, Tamada A, Nagata S, Kagamiyama H, Mori K. BIG-1: a new TAG-1/F3-related member of the immunoglobulin superfamily with neurite outgrowth-promoting activity. Neuron 1994 Aug;13(2):415-26).	Cancer, infections, autoimmune disorders, wound healing disorders and hematopoietic disorders
sbg297169-BGP	An embodiment of the invention is the use of sbg297169BGP in renewal and/or differentiation of epithelial cells. A close homologue to sbg297169BGP is BGP protein. BGP proteins are expressed at the cell surface and function *in vitro* as cell adhesion molecules. The expression of the many BGP isoforms at the surface of epithelial cells, such as the colon, suggests that these proteins play a major role in renewal and/or differentiation of their epithelia (McCuaig K, Rosenberg M, Nedellec P, Turbide C, and Beauchemin N; 1993; Gene 127:173-83).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg253919-HSCCAa	An embodiment of the invention is the use of sbg253919-HSCCAa for treatment of cancer or psoriasis or in development of more aggressive squamous cell carcinomas. Close homologues of sbg253919-HSCCAa are Psoriastatin type II and a human leupin precursor. Psoriastatin type II, is claimed to modulate activity of psoriastatin type I and II genes, e.g. using (ant)agonists, useful for treatment of cancer or psoriasis. The other, a human leupin precursor, contains a tandem duplication of the human squamous cell carcinoma antigen gene playing a causal role in development of more aggressive squamous cell carcinomas (1. Goetinck PF, Hibino T, Takahashi T and Baciu PC. Modulating cell proliferation or apoptosis - by modulating activity of psoriastatin type I and II genes, e.g. using (ant) agonists, useful for treatment of cancer or psoriasis. Accession Number W15242, publication date 24-APR-97. 2. Schneider SS, Schick C, Fish KE, Miller E, Pena JC, Treter SD, Hui SM, Silverman GA. A serine proteinase inhibitor locus at 18q21.3 contains a tandem duplication of the human squamous cell carcinoma antigen gene. Proc Natl Acad Sci U S A 1995 Apr 11;92(8):3147-51. 3. Barnes RC, Worrall DM. Identification of a novel human serpin gene; cloning sequencing and expression of leupin. FEBS Lett 1995 Oct 2; 373 (1): 61-5).	Cancers, such as squamous cell carcinomas
sbg228137-OLF	An embodiment of the invention is the use of sbg228137OLF in functinal roles in chemoreception and in the central nervous system. A close homologue to sbg228137OLF is olfactomedin. Olfactomedin is a glycoprotein, and reacts with proteins of olfactory cilia. It was originally discovered at the mucociliary surface of the amphibian olfactory neuroepithelium and subsequently found throughout the mammalian brain (Danielson,P.E., Forss-Petter,S., Battenberg,E.L., deLecea,L., Bloom,F.E., and Sutcliffe,J.G., 1994, J. Neurosci. Res. 38:468-478). Its noticeable deposition at the chemosensory surface of the olfactory neuroepithelium suggest a role for this protein in chemoreception (Snyder DA, Rivers AM, Yokoe H, Menco BP, and Anholt RR, 1991, Biochemistry 30:9143-53). The widespread occurrence of olfactomedin among mammalians in the brains also suggests its new functions in the central nervous system (Karavanich CA, and Anholt RR, 1998, Mol Biol Evol 15:718-26).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, and nervous system disorders

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg378514-Netrin	An embodiment of the invention is the use of sbg378514-Netrin in roles of the central nervous system. A close homologue to sbg378514-Netrin is Netrin. Netrins possess commissural axon outgrowth-promoting activity, and control guidance of CNS commissural axons and peripheral motor axons (Serafini T, Kennedy TE, Galko MJ, Mirzayan C, Jessell TM, and Tessier-Lavigne M; 1994; Cell 78:409-24). Diffusible and substrate-bound cues, including netrins and their receptors, can guide axonal pathway choice via attractive and repulsive signals (Tear G; 1998; Essays Biochem 33:1-13).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, and nervous system disorder
sbg253227. mucous matrix glycoprotein	An embodiment of the invention is the use of sbg253227.-mucous matrix glycoprotein for the treatment of gastrointestinal disorders and cancer. Close homologues of sbg253227.mucous matrix glycoprotein have been used in combination for treatment of infections associated with EMMG. EMMG is useful for the treatment of gastrointestinal disorders and cancer, e.g. dysphagia, abdominal angina, pancreatitis, colonic carcinoma, Crohn's disease and the Mallory-Weiss syndrome (US5929033-A, CORLEY NC, TANG YT, Submitted by INCYTE PHARM INC. Reference number, WPI; 99-429518/36, 1999).	Hematopoietic disorder, wound healing disorder, viral and bacterial infection, cancer, autoimmune diseases Neurological disorders, gastrointestinal disorders,dysphagia, abdominal angina, pancreatitis, colonic carcinoma,Crohn's disease and the Mallory-Weiss syndrome.
sbg262831-SIAa	An embodiment of the invention is the use of sbg262831SIAa to mediate sialic acid-dependent ligand recognition and to function as an inhibitory receptor in human natural killer cells. A close homologue of sbg262831SIAa is human QA79 membrane protein. QA79 belongs to the sialoadhesin family and is proposed to mediate sialic acid-dependent ligand recognition and to function as an inhibitory receptor in human natural killer cells (Falco,M., Biassoni,R., Bottino,C., Vitale,M., Sivori,S., Augugliaro,R., Moretta,L. and Moretta,A. Identification and molecular cloning of p75/AIRM1, a novel member of the sialoadhesin family that functions as an inhibitory receptor in human natural killer cells. J Exp Med 1999 Sep 20;190(6):793-802).	Cancer, autoimmune disorders, infection, wound healing disorders, and hematopoietic disorders.

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg233728-LIPASE	An embodiment of the invention is the use of sbg233728LIPASE to treat pancreatitis via replacement therapy. A close homologue of sbg233728-LIPASE is pancreatic lipase. Pancreatic lipase can be used as replacement enzymes for patients with chronic pancreatitis. Pancreatic lipase hydrolyzes dietary long chain triacylglycerol to free fatty acids and monoacylglycerols in the intestinal lumen (Lowe ME, Rosenblum JL, and Strauss AW; 1989; J Biol Chem 264:20042-8). Pancreatic steatorrhea and pancreatic diabetes are the dominant symptoms of patients in a certain stage of chronic pancreatitis. In this stage, the nutritional state is greatly disturbed and hypoglycemia and labile infection are involved. Pancreatic enzyme replacement therapy is the principal treatment method for pancreatic steatorrhea. (Nakamura T, Takeuchi T, and Tando Y; 1998; Pancreas 16:329-36).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, and pancreatitis.
sbg400455.-CRF	An embodiment of the invention is the use of sbg400455.CRF in the areas of the nervous system involved in motor function, such as the Purkinje cells of the cerebellum, the accessory olivary nucleus, the pons, and the red nucleus. Close homologues of sbg400455.CRF include CRF transcripts. CRF transcripts are most abundant in areas of the nervous system and have been used to develop products for modulating energy balance or insulin production in mammals ((W09639429-A2) Schere, P.E.; Submitted by Whithead Institute of Biomedical Research; Berube NG, Swanson XH, Bertram MJ, Kittle JD, Didenko V, Baskin DS,Smith JR and Pereira-Smith OM., Brain Res. Mol. Brain Res. 63 (2), 233-240 (1999)).	Hematopoietic disorder, wound healing disorder, viral and bacterial infection, cancer, autoimmune diseases, energy homeostasis disorder and obesity
sbg400612-KINASEa	An embodiment of the invention is the use of sbg400612-KINASEa in the treatment of inflammation, cancer, neurological diseases, growth and developmental defects, skin wounds, and hair follicle disorders. A close homologue of sbg400612-KINASEa is murine protein kinase/ ankyrin homologue. Murine protein kinase/ ankyrin homologue can stimulate the growth and motility of keratinocytes, inhibit the growth of cancer cells, modulate angiogenesis and tumour vascularisation, modulate skin inflammation and epithelial cell growth and inhibit binding of HIV-1 to leukocytes. Murine protein kinase/ ankyrin homologue can also be used to treat inflammation, cancer, neurological diseases, growth and developmental defects, skin wounds, and hair follicle disorders (Kumble A, Murison JG, Onrust R, Sleeman M, Strachan L and Watson JD. Novel polynucleotides useful for the treatment of various conditions including wounds and cancer. Accession Number: Y76079 Publication Date: 04-NOV-99).	Cancer, wound healing disorders, autoimmune disorders, hematopoietic disorders and infection

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg381373-ACRP	An embodiment of the invention is the use of sbg381373-ACRP in the complex balanced system of energy homeostasis involving food intake, carbohydrate catabolism, and lipid catabolism. A close homologue of sbg381373-ACRP is ACRP30 protein. ACRP30 protein may be a factor that participates in the complex balanced system of energy homeostasis involving food intake, carbohydrate catabolism, and lipid catabolism. ACRP30 is structurally similar to complement factor C1q, and it forms large homo-oligomers that undergo a series of post-translational modifications (Scherer PE, Williams S, Fogliano M, Baldini G, Lodish HF; 1995; J Biol Chem 270:26746-9).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, obesity, and diabetes
sbg401294-MEX-3	An embodiment of the invention is the use of sbg401294-MEX-3 to develop products for diagnosis and therapy of disease states such as tumor formation, apoptosis regulation in cells to reduce or increase apoptosis and for pharmacological screening.	Hematopoietic disorder, wound healing disorder, viral and bacterial infection, cancer, tumor formation, autoimmune diseases, inhibition of apoptosis
sbg247722-Cadherin	An embodiment of the invention is the use of sbg247722-Cadherin for treatment and diagnosis of bone metabolic diseases. A close homologue of sbg247722-Cadherin is cadherin, a Ca2+ dependent cell adhesion protein.	Hematopoietic disorder, wound healing disorder, viral and bacterial infection, cancer, autoimmune diseases, energy homeostasis disorder and bone metabolic disease
sbg391057-THIPa	An embodiment of the invention is the use of sbg391057-THIPa in controlling thyroid hormone synthesis. A close homologue of sbg391057-THIPa is xenopus laevis thyroid hormone-induced protein. Xenopus laevis thyroid hormone-induced protein has been implicated in controlling thyroid hormone synthesis in Xenopus tadpoles and provided insights into the biology of metamorphosis (Brown,D.D., Wang,Z., Furlow,J.D., Kanamori,A., Schwartzman, R.A., Remo,B.F. and Pinder,A. The thyroid hormone-induced tail resorption program during Xenopus laevis metamorphosis. Proc Natl Acad Sci U S A 1996 Mar 5;93(5):1924-9).	Autoimmune disorders, wound healing disorders, cancer, infection and hematopoietic disorders

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg378067-TGFc	An embodiment of the invention is the use of sbg378067-TGFc in cellular growth control in the etiology of cancer and cell differentiation and development. The sbg378067-TGFc protein contains a close approximation of the prosite consensus pattern (PDOC00223) for TGF-beta family members. TGF-beta proteins have been known to be involved in growth control and hence the etiology of cancer (*Anticancer Res* 1999 Nov-Dec;19(6A):4791-807), cell differentiation and development. A TGF-beta signaling pathway constitutes a tumor suppressor path (*Cytokine Growth Factor Rev* 2000 Apr 1;11(1-2):159-168). A close homologue of sbg378067-TGFc is TGF-beta protein.	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorder, inflammation, preventing or treating cellular degeneration or insufficiency, e.g. neuronal degeneration resulting from peripheral neuropathy, amyotrophic lateral sclerosis, Alzheimer's disease, Parkinson's disease, Huntington's disease, ischemic stroke, acute brain injury, acute spinal cord injury, nervous system tumours, multiple sclerosis, or infection (viral, bacterial, fungal, parasitic), hematopoietic cell degeneration or insufficiency resulting from eosinopenia, anemias, thrombocytopenia, or stem-cell insufficiences, cardiac muscle degeneration or insufficiency resulting from cardiomyopathy or congestive heart failure, peripheral nerve trauma or injury, exposure to neurotoxins, metabolic diseases such as diabetes or renal dysfunctions and damage caused by infectious agents

Table IV. Quantitative, Tissue-specific mRNA expression detected using SybrMan

Quantitative, tissue-specific, mRNA expression patterns of the genes were measured using SYBR-Green Quantitative PCR (Applied Biosystems, Foster City, CA; see Schmittgen T.D. et al., Analytical Biochemistry 285:194-204, 2000) and human cDNAs prepared from various human tissues. Gene-specific PCR primers were designed using the first nucleic acid sequence listed in the Sequence List for each gene. Results are presented as the number of copies of each specific gene's mRNA detected in 1ng mRNA pool from each tissue. Two replicate mRNA measurements were made from each tissue RNA.

Gene Name	Tissue-Specific mRNA Expression (copies per ng mRNA; avg. ± range for 2 data points per tissue)									
	Brain	Heart	Lung	Liver	Kid-ney	Skele-tal muscl e	Intes-tine	Splee n/lym ph	Pla-centa	Testis
sbg237038SA	14±1	27±1	39±1	14±0	18±1	12±0	21±3	45±2	19±3	40±9
sbg340871-GPV	0±0	200± 46	363± 10	-9±6	33±13	93±17	74±9	305±9	2902± 114	36±4
sbg293416-HNKS	553± 15	65±1	39±4	27±4	39±1	38±1	53±4	225±9	43±0	108±9
sbg257418ZP	37±3	28±6	6±0	-12±3	-4±2	19±7	15±2	5±2	10±2	605± 10
sbg319185-CDa	54±5	113±3	696± 140	95±37	317± 31	708± 30	540± 64	5987± 158	326±2	258± 31
sbg323307-KIAAa	293±8	633± 15	1269± 58	15±1	136±5	26±6	1400± 91	33±12	632± 12	196± 10
sbg315953-GPPa	232± 31	16±0	54±2	1±6	14±7	4±8	15±3	99±4	61±7	126±6
sbg318486-ONC	52±7	3±2	8±0	4±0	4±2	2±1	6±2	1±7	4±1	122±9
sbg299359-LIPO	1701± 95	39±0	60±14	21±1	135± 13	41±3	49±2	26±7	40±5	138±2

Table IV (cont.)

Gene Name	Tissue-Specific mRNA Expression (copies per ng mRNA; avg. ± range for 2 data points per tissue)									
	Brain	Heart	Lung	Liver	Kidney	Skeletal muscle	Intestine	Spleen /lymph	Placenta	Testis
sbg230022-NGa	3443±112	684±2	386±7	712±16	1956±63	36±0	588±7	1293±17	43±7	358±2
sbg297169-BGP	417±29	141±8	236±5	170±11	322±0	74±4	231±1	370±0	223±3	968±32
sbg253919-HSCCAa	-5±1	1±1	2±1	-14±2	-10±0	-4±3	0±1	6±1	4±3	119±9
sbg228137-OLF	5174±138	58±4	99±5	9±3	63±7	167±12	98±0	719±9	32±8	67±4
sbg253227. mucous matrix glycoprotein	5±0	11±1	21±1	0±1	28±2	1±0	13±2	24±3	26±4	118±1
sbg262831-SIAa	9±1	6±1	59±1	59±1	5±0	-4±2	134±6	2657±97	45±4	25±0
sbg233728-LIPASE	2±1	6±1	4±2	6±2	1±0	4±0	1±3	1±2	3±2	28±3
sbg400455.-CRF	8735±257	345±14	434±54	191±14	4038±147	705±32	379±1	847±59	434±8	97±8
sbg400612-KINASEa	10±0	24±4	276±87	145±2	431±10	7±0	59±5	23±4	82±9	34±3
sbg381373-ACRP	112±40	11±3	15±5	14±5	10±2	11±8	14±4	-3±8	6±2	11±8
sbg401294-MEX-3	49±8	39±2	122±1	35±9	151±8	6±5	16±1	15±3	71±8	683±56
sbg247722-Cadherin	2626±18	1140±22	1733±62	78±4	2007±12	213±52	1175±47	1701±167	3487±263	1814±30
sbg391057-THIPa	332±3	3010±30	8567±84	136±1	1013±90	1499±172	2469±86	3512±23	1393±32	2408±174
sbg378067-TGFc	33±8	58±6	52±4	3±1	48±1	49±22	21±4	116±28	74±24	59±4

Table V. Additional diseases based on mRNA expression in specific tissues

Tissue Expression	Additional Diseases
Brain	Neurological and psychiatric diseases, including Alzheimers, parasupranuclear palsey, Huntington's disease, myotonic dystrophy, anorexia, depression, schizophrenia, headache, amnesias, anxiety disorders, sleep disorders, multiple sclerosis
Heart	Cardiovascular diseases, including congestive heart failure, dilated cardiomyopathy, cardiac arrhythmias, Hodgson's Disease, myocardial infarction, cardiac arrhythmias
Lung	Respiratory diseases, including asthma, Chronic Obstructive Pulmonary Disease, cystic fibrosis, acute bronchitis, adult respiratory distress syndrome
Liver	Dyslipidemia, hypercholesterolemia, hypertriglyceridemia, cirrhosis, hepatic encephalopathy, fatty hepatocirrhosis, viral and nonviral hepatitis, Type II Diabetes Mellitis, impaired glucose tolerance
Kidney	Renal diseases, including acute and chronic renal failure, acute tubular necrosis, cystinuria, Fanconi's Syndrome, glomerulonephritis, renal cell carcinoma, renovascular hypertension
Skeletal muscle	Eulenburg's Disease, hypoglycemia, obesity, tendinitis, periodic paralyses, malignant hyperthermia, paramyotonia congenita, myotonia congenita
Intestine	Gastrointestinal diseases, including Myotonia congenita, Ileus, Intestinal Obstruction, Tropical Sprue, Pseudomembranous Enterocolitis
Spleen/lymph	Lymphangiectasia, hypersplenism, angiomas, ankylosing spondylitis, Hodgkin's Disease, macroglobulinemia, malignant lymphomas, rheumatoid arthritis
Placenta	Choriocarcinoma, hydatidiform mole, placenta previa
Testis	Testicular cancer, male reproductive diseases, including low testosterone and male infertility
Pancreas	Diabetic ketoacidosis, Type 1 & 2 diabetes, obesity, impaired glucose tolerance

What is claimed is:

1. An isolated polypeptide selected from the group consisting of:
(a) an isolated polypeptide encoded by a polynucleotide comprising a sequence set forth in Table I;
(b) an isolated polypeptide comprising a polypeptide sequence set forth in Table I; and
(c) a polypeptide sequence of a gene set forth in Table I.

2. An isolated polynucleotide selected from the group consisting of:
(a) an isolated polynucleotide comprising a polynucleotide sequence set forth in Table I;
(b) an isolated polynucleotide of a gene set forth in Table I;
(c) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide set forth in Table I;
(d) an isolated polynucleotide encoding a polypeptide set forth in Table I;
(e) a polynucleotide which is an RNA equivalent of the polynucleotide of (a) to (d);
or a polynucleotide sequence complementary to said isolated polynucleotide.

3. An expression vector comprising a polynucleotide capable of producing a polypeptide of claim 1 when said expression vector is present in a compatible host cell.

4. A process for producing a recombinant host cell which comprises the step of introducing an expression vector comprising a polynucleotide capable of producing a polypeptide of claim 1 into a cell such that the host cell, under appropriate culture conditions, produces said polypeptide.

5. A recombinant host cell produced by the process of claim 4.

6. A membrane of a recombinant host cell of claim 5 expressing said polypeptide.

7. A process for producing a polypeptide which comprises culturing a host cell of claim 5 under conditions sufficient for the production of said polypeptide and recovering said polypeptide from the culture.

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<212> DNA

<213> Homo sapiens

<400> 35

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<211> 2346
<212> DNA
<213> Homo sapiens

<400> 36

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<211> 1923
<212> DNA
<213> Homo sapiens

<400> 37
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<210> 38
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<212> DNA
<213> Homo sapiens

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<210> 39
<211> 465
<212> DNA
<213> Homo sapiens

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<210> 40
<211> 277
<212> PRT
<213> Homo sapiens

<400> 40

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            20                  25                  30
Ala Lys Leu Thr Lys Glu Ser Val Met Asp Thr Leu Val Gln Ile Leu
        35                  40                  45
Ala Arg Cys Asp Ile Met Val Leu Gln Glu Val Val Asp Ser Ser Gln
    50                  55                  60
Asn Thr Val Pro Phe Leu Leu Gln Lys Leu Lys Ser Ser Arg Ser Tyr
65                  70                  75                  80
Ser Phe Leu Asn Ser Ser Leu Leu Gly Arg Ser Thr Tyr Lys Glu Lys
                85                  90                  95
Tyr Val Tyr Ile Tyr Arg Ser Asp Lys Thr Gln Val Leu Asn Phe Tyr
            100                 105                 110
Gln Tyr Asn Asp Thr Asp Asp Ile Phe Ala Arg Glu Pro Phe Val Ala
        115                 120                 125
His Phe Thr Leu Pro Ser Lys Thr Leu Pro Ser Val Val Leu Val Pro
    130                 135                 140
Leu His Thr Thr Pro Lys Asp Val Glu Lys Glu Leu Asn Ala Leu Tyr
145                 150                 155                 160
Asp Val Phe Leu Asp Val Tyr Gln Arg Trp Gln Asn Glu Asn Val Ile
                165                 170                 175
Leu Leu Gly Asp Phe Asn Ala Asp Cys Ala Ser Leu Thr Lys Lys Arg
            180                 185                 190
Leu Lys Ser Leu Leu Leu Arg Thr Lys Ala Gly Phe His Trp Val Ile
        195                 200                 205
Pro Asp Gly Glu Asp Thr Thr Val Arg Ala Ser Thr Asn Cys Thr Tyr
    210                 215                 220
Asp Arg Ile Val Val His Gly Gln Gly Cys Gln Met Leu Leu Lys Ala
225                 230                 235                 240
Ala Ala Thr Phe Asp Phe Pro Lys Arg Phe Gln Leu Thr Glu Glu Glu
                245                 250                 255
Ala Leu Arg Ile Ser Asp His Tyr Pro Val Glu Val Glu Leu Ser Gln
            260                 265                 270
Ala Thr Pro Leu Ser
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<210> 41
<211> 480
<212> PRT
<213> Homo sapiens

<400> 41

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Gly Phe Gly Ala Cys Cys Tyr Pro Asn Gln Lys Cys Ala Thr Gln Thr
            20                  25                  30
Ile Arg Pro Pro Asp Ser Arg Cys Leu Val Gln Ala Val Ser Gln Asn
        35                  40                  45
Phe Asn Phe Ala Lys Asp Val Leu Asp Gln Trp Ser Gln Leu Glu Lys
    50                  55                  60
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Asp Gly Leu Arg Gly Pro Tyr Pro Ala Leu Trp Lys Val Ser Ala Lys
65                  70                  75                  80
Gly Glu Glu Asp Lys Trp Ser Phe Glu Arg Met Thr Gln Leu Ser Lys
                85                  90                  95
Lys Ala Ala Ser Ile Leu Ser Asp Thr Cys Ala Leu Ser His Gly Asp
            100                 105                 110
Arg Leu Met Ile Ile Leu Pro Pro Thr Pro Glu Ala Tyr Trp Ile Cys
        115                 120                 125
Leu Ala Cys Val Arg Leu Gly Ile Thr Phe Val Pro Gly Ser Pro Gln
    130                 135                 140
Leu Thr Ala Lys Lys Ile Arg Tyr Gln Leu Arg Met Ser Lys Ala Gln
145                 150                 155                 160
Cys Ile Val Ala Asn Glu Ala Met Ala Pro Val Val Asn Ser Ala Val
                165                 170                 175
Ser Asp Cys Pro Thr Leu Lys Thr Lys Leu Leu Val Ser Asp Lys Ser
            180                 185                 190
Tyr Asp Gly Trp Leu Asp Phe Lys Lys Leu Ile Gln Val Ala Pro Pro
        195                 200                 205
Lys Gln Thr Tyr Met Arg Thr Lys Ser Gln Asp Pro Met Ala Ile Phe
    210                 215                 220
Phe Thr Lys Gly Thr Thr Gly Ala Pro Lys Met Val Glu Tyr Ser Gln
225                 230                 235                 240
Tyr Gly Leu Gly Met Gly Phe Ser Gln Ala Ser Arg Arg Trp Met Asp
                245                 250                 255
Leu Gln Pro Thr Asp Val Leu Trp Ser Leu Gly Asp Ala Phe Gly Gly
            260                 265                 270
Ser Leu Ser Leu Ser Ala Val Leu Gly Thr Trp Phe Gln Gly Ala Cys
        275                 280                 285
Val Phe Leu Cys His Met Pro Thr Phe Cys Pro Glu Thr Val Leu Asn
    290                 295                 300
Val Leu Ser Arg Phe Pro Ile Thr Thr Leu Ser Ala Asn Pro Glu Met
305                 310                 315                 320
Tyr Gln Glu Leu Leu Gln His Lys Cys Phe Thr Ser Tyr Arg Phe Lys
                325                 330                 335
Ser Leu Lys Gln Cys Val Ala Ala Gly Gly Pro Ile Ser Pro Gly Val
            340                 345                 350
Ile Glu Asp Trp Lys Arg Ile Thr Lys Leu Asp Ile Tyr Glu Gly Tyr
        355                 360                 365
Gly Gln Thr Glu Thr Gly Leu Leu Cys Ala Thr Ser Lys Thr Ile Lys
    370                 375                 380
Leu Lys Pro Ser Ser Leu Gly Lys Pro Leu Pro Pro Tyr Ile Val Gln
385                 390                 395                 400
Ile Val Asp Glu Asn Ser Asn Leu Leu Pro Pro Gly Glu Glu Gly Asn
                405                 410                 415
Ile Ala Ile Arg Ile Lys Leu Asn Gln Pro Ala Ser Leu Tyr Cys Pro
            420                 425                 430
His Met Val Ser Trp Glu Glu Tyr Ala Ser Ala Arg Gly His Met Leu
        435                 440                 445
Tyr Leu Thr Gly Asp Arg Gly Ile Met Asp Glu Asp Gly Tyr Phe Trp
    450                 455                 460
Trp Ser Gly Arg Val Asp Asp Val Ala Asn Ala Leu Gly Gln Arg Leu
465                 470                 475                 480
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<210> 42
<211> 583
<212> PRT
<213> Homo sapiens

<400> 42

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            20                  25                  30
Ile Arg Pro Pro Asp Ser Arg Cys Leu Val Gln Ala Val Ser Gln Asn
        35                  40                  45
Phe Asn Phe Ala Lys Asp Val Leu Asp Gln Trp Ser Gln Leu Glu Lys
    50                  55                  60
Asp Gly Leu Arg Gly Pro Tyr Pro Ala Leu Trp Lys Val Ser Ala Lys
65                  70                  75                  80
Gly Glu Glu Asp Lys Trp Ser Phe Glu Arg Met Thr Gln Leu Ser Lys
                85                  90                  95
Lys Ala Ala Ser Ile Leu Ser Asp Thr Cys Ala Leu Ser His Gly Asp
            100                 105                 110
Arg Leu Met Ile Ile Leu Pro Pro Thr Pro Glu Ala Tyr Trp Ile Cys
        115                 120                 125
Leu Ala Cys Val Arg Leu Gly Ile Thr Phe Val Pro Gly Ser Pro Gln
    130                 135                 140
Leu Thr Ala Lys Lys Ile Arg Tyr Gln Leu Arg Met Ser Lys Ala Gln
145                 150                 155                 160
Cys Ile Val Ala Asn Glu Ala Met Ala Pro Val Val Asn Ser Ala Val
                165                 170                 175
Ser Asp Cys Pro Thr Leu Lys Thr Lys Leu Leu Val Ser Asp Lys Ser
            180                 185                 190
Tyr Asp Gly Trp Leu Asp Phe Lys Lys Leu Ile Gln Val Ala Pro Pro
        195                 200                 205
Lys Gln Thr Tyr Met Arg Thr Lys Ser Gln Asp Pro Met Ala Ile Phe
    210                 215                 220
Phe Thr Lys Gly Thr Thr Gly Ala Pro Lys Met Val Glu Tyr Ser Gln
225                 230                 235                 240
Tyr Gly Leu Gly Met Gly Phe Ser Gln Ala Ser Arg Arg Trp Met Asp
                245                 250                 255
Leu Gln Pro Thr Asp Val Leu Trp Ser Leu Gly Asp Ala Phe Gly Gly
            260                 265                 270
Ser Leu Ser Leu Ser Ala Val Leu Gly Thr Trp Phe Gln Gly Ala Cys
        275                 280                 285
Val Phe Leu Cys His Met Pro Thr Phe Cys Pro Glu Thr Val Leu Asn
    290                 295                 300
Val Leu Ser Arg Phe Pro Ile Thr Thr Leu Ser Ala Asn Pro Glu Met
305                 310                 315                 320
Tyr Gln Glu Leu Leu Gln His Lys Cys Phe Thr Ser Tyr Arg Phe Lys
                325                 330                 335
Ser Leu Lys Gln Cys Val Ala Ala Gly Gly Pro Ile Ser Pro Gly Val
            340                 345                 350
Ile Glu Asp Trp Lys Arg Ile Thr Lys Leu Asp Ile Tyr Glu Gly Tyr
        355                 360                 365
Gly Gln Thr Glu Thr Gly Leu Leu Cys Ala Thr Ser Lys Thr Ile Lys
    370                 375                 380
Leu Lys Pro Ser Ser Leu Gly Lys Pro Leu Pro Pro Tyr Ile Val Gln
385                 390                 395                 400
Ile Val Asp Glu Asn Ser Asn Leu Leu Pro Pro Gly Glu Glu Gly Asn
                405                 410                 415
Ile Ala Ile Arg Ile Lys Leu Asn Gln Pro Ala Ser Leu Tyr Cys Pro
            420                 425                 430
His Met Val Ser Trp Glu Glu Tyr Ala Ser Ala Arg Gly His Met Leu
        435                 440                 445
Tyr Leu Thr Gly Asp Arg Gly Ile Met Asp Glu Asp Gly Tyr Phe Trp
    450                 455                 460
Trp Ser Gly Arg Val Asp Asp Val Ala Asn Ala Leu Gly Gln Arg Phe
```

```
465                 470                 475                 480
Ser Arg Pro Gly Ala Ala Ala Ala Ala Ser Ala Val Gly Ala Pro Pro
                485                 490                 495
Gly Gly Trp His Ser Leu Cys Ala Ser Val Pro Ile Leu Gln Val Val
            500                 505                 510
Lys Pro Pro Asn Val Leu Thr Pro Gln Phe Leu Ser His Asp Gln Gly
        515                 520                 525
Gln Leu Thr Lys Glu Leu Gln Gln His Ile Lys Ser Val Thr Gly Pro
    530                 535                 540
Cys Lys Tyr Gln Arg Lys Val Glu Phe Val Pro Glu Leu Pro Lys Thr
545                 550                 555                 560
Val Thr Gly Lys Ile Lys Arg Glu Leu Gln Val Trp Ser Asp Val Val
                565                 570                 575
Ser Ser Glu Leu Arg Asn Asp
            580
```

<210> 43
<211> 581
<212> PRT
<213> Homo sapiens

<400> 43

```
Met Pro Leu Lys His Tyr Leu Leu Leu Leu Val Gly Cys Gln Ala Trp
 1               5                  10                  15
Gly Ala Gly Leu Ala Tyr His Gly Cys Pro Ser Glu Cys Thr Cys Ser
            20                  25                  30
Arg Ala Ser Gln Val Glu Cys Thr Gly Ala Arg Ile Val Ala Val Pro
        35                  40                  45
Thr Pro Leu Pro Trp Asn Ala Met Ser Leu Gln Ile Leu Asn Thr His
    50                  55                  60
Ile Thr Glu Leu Asn Glu Ser Pro Phe Leu Asn Ile Ser Ala Leu Ile
65                  70                  75                  80
Ala Leu Arg Ile Glu Lys Asn Glu Leu Ser Arg Ile Thr Pro Gly Ala
                85                  90                  95
Phe Arg Asn Leu Gly Ser Leu Arg Tyr Leu Ser Leu Ala Asn Asn Lys
            100                 105                 110
Leu Gln Val Leu Pro Ile Gly Leu Phe Gln Gly Leu Asp Ser Leu Glu
        115                 120                 125
Ser Leu Leu Leu Ser Ser Asn Gln Leu Leu Gln Ile Gln Pro Ala His
    130                 135                 140
Phe Ser Gln Cys Ser Asn Leu Lys Glu Leu Gln Leu His Gly Asn His
145                 150                 155                 160
Leu Glu Tyr Ile Pro Asp Gly Ala Phe Asp His Leu Val Gly Leu Thr
                165                 170                 175
Lys Leu Asn Leu Gly Lys Asn Ser Leu Thr His Ile Ser Pro Arg Val
            180                 185                 190
Phe Gln His Leu Gly Asn Leu Gln Val Leu Arg Leu Tyr Glu Asn Arg
        195                 200                 205
Leu Thr Asp Ile Pro Met Gly Thr Phe Asp Gly Leu Val Asn Leu Gln
    210                 215                 220
Glu Leu Ala Leu Gln Gln Asn Gln Ile Gly Leu Leu Ser Pro Gly Leu
225                 230                 235                 240
Phe His Asn Asn His Asn Leu Gln Arg Leu Tyr Leu Ser Asn Asn His
                245                 250                 255
Ile Ser Gln Leu Pro Pro Ser Ile Phe Met Gln Leu Pro Gln Leu Asn
            260                 265                 270
Arg Leu Thr Leu Phe Gly Asn Ser Leu Lys Glu Leu Ser Leu Gly Ile
        275                 280                 285
Phe Gly Pro Met Pro Asn Leu Arg Glu Leu Trp Leu Tyr Asp Asn His
```

```
    290                 295                 300
Ile Ser Ser Leu Pro Asp Asn Val Phe Ser Asn Leu Arg Gln Leu Gln
305                 310                 315                 320
Val Leu Ile Leu Ser Arg Asn Gln Ile Ser Phe Ile Ser Pro Gly Ala
                325                 330                 335
Phe Asn Gly Leu Thr Glu Leu Arg Glu Leu Ser Leu His Thr Asn Ala
            340                 345                 350
Leu Gln Asp Leu Asp Gly Asn Val Phe Arg Met Leu Ala Asn Leu Gln
        355                 360                 365
Asn Ile Ser Leu Gln Asn Asn Arg Leu Arg Gln Leu Pro Gly Asn Ile
    370                 375                 380
Phe Ala Asn Val Asn Gly Leu Met Ala Ile Gln Leu Gln Asn Asn Gln
385                 390                 395                 400
Leu Glu Asn Leu Pro Leu Gly Ile Phe Asp His Leu Gly Lys Leu Cys
                405                 410                 415
Glu Leu Arg Leu Tyr Asp Asn Pro Trp Arg Cys Asp Ser Asp Ile Leu
            420                 425                 430
Pro Leu Arg Asn Trp Leu Leu Leu Asn Gln Pro Arg Leu Gly Thr Asp
        435                 440                 445
Thr Val Pro Val Cys Phe Ser Pro Ala Asn Val Arg Gly Gln Ser Leu
    450                 455                 460
Ile Ile Ile Asn Val Asn Val Ala Val Pro Ser Val His Val Pro Glu
465                 470                 475                 480
Val Pro Ser Tyr Pro Glu Thr Pro Trp Tyr Pro Asp Thr Pro Ser Tyr
                485                 490                 495
Pro Asp Thr Thr Ser Val Ser Ser Thr Thr Glu Leu Thr Ser Pro Val
            500                 505                 510
Glu Asp Tyr Thr Asp Leu Thr Thr Ile Gln Val Thr Asp Asp Arg Ser
        515                 520                 525
Val Trp Gly Met Thr His Ala His Ser Gly Leu Ala Ile Ala Ala Ile
    530                 535                 540
Val Ile Gly Ile Val Ala Leu Ala Cys Ser Leu Ala Ala Cys Val Gly
545                 550                 555                 560
Cys Cys Cys Cys Lys Lys Arg Ser Gln Ala Val Leu Met Gln Met Lys
                565                 570                 575
Ala Pro Asn Glu Cys
            580
```

<210> 44
<211> 628
<212> PRT
<213> Homo sapiens

<400> 44

```
Met Pro Gly Ala Pro Asp Trp Ser Leu Asn Ser Ser Arg Asn Ala Arg
 1               5                  10                  15
Ser Leu Glu Gly Leu Pro Leu Cys Pro Trp Trp Ala Leu Phe Val Pro
            20                  25                  30
Arg Ala Ala Ala Leu Val Gly Leu Gln Arg Lys Gln Glu Asn Ser Ser
        35                  40                  45
Asp Ile Phe Phe Ser Ser Pro Phe Thr Val Thr Pro Asp Ala Leu Pro
    50                  55                  60
Thr Ala Ile Thr Trp Glu His Ile Pro Phe Ala Lys Leu Ala Gly Leu
65                  70                  75                  80
Ile Ala Gly Pro Leu Val Glu Met Cys Arg Gln Arg Leu Ser Lys Glu
                85                  90                  95
Phe Glu Ala Leu Lys Gly Glu Phe Arg Asp Leu Gly His Cys Leu Pro
            100                 105                 110
Gly Ala Gln Arg Gly Asn Arg Ile Thr Lys Arg Asn Lys Cys Gly Gln
```

```
        115                 120                 125
Ser Arg Gln Ala Leu Ile Gly Gln Arg Gln Glu Asp Ala Gly Ser Ala
    130                 135                 140
Pro Leu Gln Met His Pro Ser Val Ala Ala Leu Gly Ala Gly Ala Ala
145                 150                 155                 160
Leu Arg Glu Ile Gln Pro Leu Gln Arg Glu Pro Glu Leu Ser Ser Gly
                165                 170                 175
Pro Arg Asn Ser Arg Leu Leu Cys Trp Gly Ser Pro Ala Thr Trp Asn
            180                 185                 190
Pro Thr Tyr Leu Ser Arg Val Leu Gly Gln Gln Val Ala Val Thr Val
        195                 200                 205
Thr Glu Ala Gly Leu Gln Ala Val Pro Trp Gly Pro Ser Arg Glu Phe
    210                 215                 220
Asn Ala Lys Gly Ser Ser Ser Ala Ser Ile Arg Val Gly Gln Pro Gln
225                 230                 235                 240
Lys Leu Arg Leu Arg Val Gln Arg Ser Arg Arg Gln Cys Pro Pro Val
                245                 250                 255
Gln Ser Ser Gln Asp Leu Pro Pro Gly Gly Ser Gln Asp Gly Asp Leu
            260                 265                 270
Lys Glu Pro Thr Glu Arg Val Thr Arg Asp Leu Ser Ser Gly Ala Pro
        275                 280                 285
Arg Gly Arg Asn Leu Pro Ala Pro Asp Gln Pro Gln Pro Pro Leu Gln
    290                 295                 300
Arg Gly Thr Arg Leu Arg Leu Arg Gln Arg Arg Arg Arg Leu Leu Ile
305                 310                 315                 320
Lys Lys Met Pro Ala Ala Ala Thr Ile Pro Ala Asn Ser Ser Asp Ala
                325                 330                 335
Pro Phe Ile Arg Pro Gly Pro Gly Thr Leu Asp Gly Arg Trp Val Ser
            340                 345                 350
Leu His Arg Ser Gln Gln Glu Arg Lys Arg Val Met Gln Glu Ala Cys
        355                 360                 365
Ala Lys Tyr Arg Ala Ser Ser Ser Arg Arg Ala Val Thr Pro Arg His
    370                 375                 380
Val Ser Arg Ile Phe Val Glu Asp Arg His Arg Val Leu Tyr Cys Glu
385                 390                 395                 400
Val Pro Lys Ala Gly Cys Ser Asn Trp Lys Arg Val Leu Met Val Leu
                405                 410                 415
Ala Gly Leu Ala Ser Ser Thr Ala Asp Ile Gln His Asn Thr Val His
            420                 425                 430
Tyr Gly Ser Ala Leu Lys Arg Leu Asp Thr Phe Asp Arg Gln Gly Ile
        435                 440                 445
Leu His Arg Leu Ser Thr Tyr Thr Lys Met Leu Phe Val Arg Glu Pro
    450                 455                 460
Phe Glu Arg Leu Val Ser Ala Phe Arg Asp Lys Phe Glu His Pro Asn
465                 470                 475                 480
Ser Tyr Tyr His Pro Val Phe Gly Lys Ala Ile Leu Ala Arg Tyr Arg
                485                 490                 495
Ala Asn Ala Ser Arg Glu Ala Leu Arg Thr Gly Ser Gly Val Arg Phe
            500                 505                 510
Pro Glu Phe Val Gln Tyr Leu Leu Asp Val His Arg Pro Val Gly Met
        515                 520                 525
Asp Ile His Trp Asp His Val Ser Arg Leu Cys Ser Pro Cys Leu Ile
    530                 535                 540
Asp Tyr Asp Phe Val Gly Lys Phe Glu Ser Met Glu Asp Asp Ala Asn
545                 550                 555                 560
Phe Phe Leu Ser Leu Ile Arg Ala Pro Arg Asn Leu Thr Phe Pro Arg
                565                 570                 575
Phe Lys Asp Arg His Ser Gln Glu Ala Arg Thr Thr Ala Arg Ile Ala
            580                 585                 590
```

```
His Gln Tyr Phe Ala Gln Leu Ser Ala Leu Gln Arg Gln Arg Thr Tyr
        595                 600                 605
Asp Phe Tyr Tyr Met Asp Tyr Leu Met Phe Asn Tyr Ser Lys Pro Phe
    610                 615                 620
Ala Asp Leu Tyr
625
```

<210> 45
<211> 424
<212> PRT
<213> Homo sapiens

<400> 45

```
Met Thr Leu Arg Pro Gly Thr Met Arg Leu Ala Cys Met Phe Ser Ser
 1               5                  10                  15
Ile Leu Leu Phe Gly Ala Ala Gly Leu Leu Leu Phe Ile Ser Leu Gln
            20                  25                  30
Asp Pro Thr Glu Leu Ala Pro Gln Gln Val Pro Gly Ile Lys Phe Asn
        35                  40                  45
Ile Arg Pro Arg Gln Pro His His Asp Leu Pro Pro Gly Gly Ser Gln
    50                  55                  60
Asp Gly Asp Leu Lys Glu Pro Thr Glu Arg Val Thr Arg Asp Leu Ser
65                  70                  75                  80
Ser Gly Ala Pro Arg Gly Arg Asn Leu Pro Ala Pro Asp Gln Pro Gln
                85                  90                  95
Pro Pro Leu Gln Arg Gly Thr Arg Leu Arg Leu Arg Gln Arg Arg Arg
            100                 105                 110
Arg Leu Leu Ile Lys Lys Met Pro Ala Ala Ala Thr Ile Pro Ala Asn
        115                 120                 125
Ser Ser Asp Ala Pro Phe Ile Arg Pro Gly Pro Gly Thr Leu Asp Gly
    130                 135                 140
Arg Trp Val Ser Leu His Arg Ser Gln Gln Glu Arg Lys Arg Val Met
145                 150                 155                 160
Gln Glu Ala Cys Ala Lys Tyr Arg Ala Ser Ser Ser Arg Arg Ala Val
                165                 170                 175
Thr Pro Arg His Val Ser Arg Ile Phe Val Glu Asp Arg His Arg Val
            180                 185                 190
Leu Tyr Cys Glu Val Pro Lys Ala Gly Cys Ser Asn Trp Lys Arg Val
        195                 200                 205
Leu Met Val Leu Ala Gly Leu Ala Ser Ser Thr Ala Asp Ile Gln His
    210                 215                 220
Asn Thr Val His Tyr Gly Ser Ala Leu Lys Arg Leu Asp Thr Phe Asp
225                 230                 235                 240
Arg Gln Gly Ile Leu His Arg Leu Ser Thr Tyr Thr Lys Met Leu Phe
                245                 250                 255
Val Arg Glu Pro Phe Glu Arg Leu Val Ser Ala Phe Arg Asp Lys Phe
            260                 265                 270
Glu His Pro Asn Ser Tyr Tyr His Pro Val Phe Gly Lys Ala Ile Leu
        275                 280                 285
Ala Arg Tyr Arg Ala Asn Ala Ser Arg Glu Ala Leu Arg Thr Gly Ser
    290                 295                 300
Gly Val Arg Phe Pro Glu Phe Val Gln Tyr Leu Leu Asp Val His Arg
305                 310                 315                 320
Pro Val Gly Met Asp Ile His Trp Asp His Val Ser Arg Leu Cys Ser
                325                 330                 335
Pro Cys Leu Ile Asp Tyr Asp Phe Val Gly Lys Phe Glu Ser Met Glu
            340                 345                 350
Asp Asp Ala Asn Phe Phe Leu Ser Leu Ile Arg Ala Pro Arg Asn Leu
        355                 360                 365
```

```
Thr Phe Pro Arg Phe Lys Asp Arg His Ser Gln Glu Ala Arg Thr Thr
    370                 375                 380
Ala Arg Ile Ala His Gln Tyr Phe Ala Gln Leu Ser Ala Leu Gln Arg
385                 390                 395                 400
Gln Arg Thr Tyr Asp Phe Tyr Tyr Met Asp Tyr Leu Met Phe Asn Tyr
                405                 410                 415
Ser Lys Pro Phe Ala Asp Leu Tyr
            420
```

<210> 46
<211> 638
<212> PRT
<213> Homo sapiens

<400> 46

```
Met Ala Gly Gly Ser Ala Thr Thr Trp Gly Tyr Pro Val Ala Leu Leu
 1                5                  10                  15
Leu Leu Val Ala Thr Leu Gly Leu Gly Arg Trp Leu Gln Pro Asp Pro
            20                  25                  30
Gly Leu Pro Gly Leu Arg His Ser Tyr Asp Cys Gly Ile Lys Gly Met
        35                  40                  45
Gln Leu Leu Val Phe Pro Arg Pro Gly Gln Thr Leu Arg Phe Lys Val
    50                  55                  60
Val Asp Glu Phe Gly Asn Arg Phe Asp Val Asn Asn Cys Ser Ile Cys
65                  70                  75                  80
Tyr His Trp Val Thr Ser Arg Pro Gln Glu Pro Ala Val Phe Ser Ala
                85                  90                  95
Asp Tyr Arg Gly Cys His Val Leu Glu Lys Asp Gly Arg Phe His Leu
            100                 105                 110
Arg Val Phe Met Glu Ala Val Leu Pro Asn Gly Arg Val Asp Val Ala
        115                 120                 125
Gln Asp Ala Thr Leu Ile Cys Pro Lys Pro Asp Pro Ser Arg Thr Leu
    130                 135                 140
Asp Ser Gln Leu Ala Pro Pro Ala Met Phe Ser Val Ser Thr Pro Gln
145                 150                 155                 160
Thr Leu Ser Phe Leu Pro Thr Ser Gly His Thr Ser Gln Gly Ser Gly
                165                 170                 175
His Ala Phe Pro Ser Pro Leu Asp Pro Gly His Ser Ser Val His Pro
            180                 185                 190
Thr Pro Ala Leu Pro Ser Pro Gly Pro Gly Pro Thr Leu Ala Thr Leu
        195                 200                 205
Ala Gln Pro His Trp Gly Thr Leu Glu His Trp Asp Val Asn Lys Arg
    210                 215                 220
Asp Tyr Ile Gly Thr His Leu Ser Gln Glu Gln Cys Gln Val Ala Ser
225                 230                 235                 240
Gly His Leu Pro Cys Ile Val Arg Arg Thr Ser Lys Glu Ala Cys Gln
                245                 250                 255
Gln Ala Gly Cys Cys Tyr Asp Asn Thr Arg Glu Val Pro Cys Tyr Tyr
            260                 265                 270
Gly Asn Thr Ala Thr Val Gln Cys Phe Arg Asp Gly Tyr Phe Val Leu
        275                 280                 285
Val Val Ser Gln Glu Met Ala Leu Thr His Arg Ile Thr Leu Ala Asn
    290                 295                 300
Ile His Leu Ala Tyr Ala Pro Thr Ser Cys Ser Pro Thr Gln His Thr
305                 310                 315                 320
Glu Ala Phe Val Val Phe Tyr Phe Pro Leu Thr His Cys Gly Thr Thr
                325                 330                 335
Met Gln Val Ala Gly Asp Gln Leu Ile Tyr Glu Asn Trp Leu Val Ser
            340                 345                 350
```

```
Gly Ile His Ile Gln Lys Gly Pro Gln Gly Ser Ile Thr Arg Asp Ser
        355                 360                 365
Thr Phe Gln Leu His Val Arg Cys Val Phe Asn Ala Ser Asp Phe Leu
    370                 375                 380
Pro Ile Gln Ala Ser Ile Phe Pro Pro Pro Ser Pro Ala Pro Met Thr
385                 390                 395                 400
Gln Pro Gly Pro Leu Arg Leu Glu Leu Arg Ile Ala Lys Asp Glu Thr
                405                 410                 415
Phe Ser Ser Tyr Tyr Gly Glu Asp Asp Tyr Pro Ile Val Arg Leu Leu
            420                 425                 430
Arg Glu Pro Val His Val Glu Val Arg Leu Leu Gln Arg Thr Asp Pro
        435                 440                 445
Asn Leu Val Leu Leu Leu His Gln Cys Trp Gly Ala Pro Ser Ala Asn
    450                 455                 460
Pro Phe Gln Gln Pro Gln Trp Pro Ile Leu Ser Asp Gly Cys Pro Phe
465                 470                 475                 480
Lys Gly Asp Ser Tyr Arg Thr Gln Met Val Ala Leu Asp Gly Ala Thr
                485                 490                 495
Pro Phe Gln Ser His Tyr Gln Arg Phe Thr Val Ala Thr Phe Ala Leu
            500                 505                 510
Leu Asp Ser Gly Ser Gln Arg Ala Leu Arg Gly Leu Val Tyr Leu Phe
        515                 520                 525
Cys Ser Thr Ser Ala Cys His Thr Ser Gly Leu Glu Thr Cys Ser Thr
    530                 535                 540
Ala Cys Ser Thr Gly Thr Thr Arg Gln Arg Arg Ser Ser Gly His Arg
545                 550                 555                 560
Asn Asp Thr Ala Arg Pro Gln Asp Ile Val Ser Ser Pro Gly Pro Val
                565                 570                 575
Gly Phe Glu Asp Ser Tyr Gly Gln Glu Pro Thr Leu Gly Pro Thr Asp
            580                 585                 590
Ser Asn Gly Asn Ser Ser Leu Arg Pro Leu Leu Trp Ala Val Leu Leu
        595                 600                 605
Leu Pro Ala Val Ala Leu Val Leu Gly Phe Gly Val Phe Val Gly Leu
    610                 615                 620
Ser Gln Thr Trp Ala Gln Lys Leu Trp Glu Ser Asn Arg Gln
625                 630                 635
```

<210> 47
<211> 229
<212> PRT
<213> *Homo sapiens*

<400> 47

```
Met Lys Pro Leu Ala Gln Leu Leu Leu Phe Leu Leu Gln Phe Gln Lys
 1               5                  10                  15
Gly Asn Leu Val Ser Gln Ser Ser Ser Thr Pro Leu Met Val Asn Gly
            20                  25                  30
Val Leu Gly Glu Ser Val Thr Leu Pro Leu Glu Phe Pro Ala Gly Glu
        35                  40                  45
Arg Ile Gln Phe Ile Thr Trp Leu Cys Asn Gly Thr Ser Phe Ala Phe
    50                  55                  60
Leu Glu Pro Tyr Glu Gly Lys Ser Pro Lys Ile Tyr Val Thr His Pro
65                  70                  75                  80
Lys Trp Gln Lys Arg Leu Ser Phe Thr Gln Ser Tyr Ser Pro Gln Leu
                85                  90                  95
Ser Asn Leu Glu Met Glu Asn Ile Gly Phe Tyr Ser Ala Gln Ile Ala
            100                 105                 110
Thr Glu Thr Ser Ala Lys Leu Ser Ser Tyr Thr Leu Arg Ile Phe Lys
        115                 120                 125
```

```
Gln Leu Pro Arg Pro Gln Val Arg Val Asp Ser Ile Ile Ser Glu Asn
    130                 135                 140
Gly Ile Cys Asn Ala Ile Leu Arg Cys Ser Val Glu Glu Gly Gly Glu
145                 150                 155                 160
Thr Ile Thr Tyr Glu Trp Thr Ser Met Gly Pro Gly Ala Ala Val Ser
                165                 170                 175
His Val Gly Leu His Asp Leu Asp Trp Ile Tyr Thr Cys Thr Ala Leu
            180                 185                 190
Asn Pro Val Ser Tyr Ser Asn Ser Thr Leu Thr Leu Ala Ala Gln Leu
        195                 200                 205
Cys Ala Ser Lys Ser Pro Leu Leu Val Ser Leu Ala Pro Leu Gly Asn
    210                 215                 220
Val Leu Ser Gly Leu
225
```

<210> 48
<211> 310
<212> PRT
<213> Homo sapiens

<400> 48

```
Met Lys Pro Leu Ala Gln Leu Leu Leu Phe Leu Leu Gln Phe Gln Lys
 1               5                  10                  15
Gly Asn Leu Val Ser Gln Ser Ser Ser Thr Pro Leu Met Val Asn Gly
            20                  25                  30
Val Leu Gly Glu Ser Val Thr Leu Pro Leu Glu Phe Pro Ala Gly Glu
        35                  40                  45
Arg Ile Gln Phe Ile Thr Trp Leu Cys Asn Gly Thr Ser Phe Ala Phe
    50                  55                  60
Leu Glu Pro Tyr Glu Gly Lys Ser Pro Lys Ile Tyr Val Thr His Pro
65                  70                  75                  80
Lys Trp Gln Lys Arg Leu Ser Phe Thr Gln Ser Tyr Ser Pro Gln Leu
                85                  90                  95
Ser Asn Leu Glu Met Glu Asn Ile Gly Phe Tyr Ser Ala Gln Ile Ala
            100                 105                 110
Thr Glu Thr Ser Ala Lys Leu Ser Ser Tyr Thr Leu Arg Ile Phe Lys
        115                 120                 125
Gln Leu Pro Arg Pro Gln Val Arg Val Asp Ser Ile Ile Ser Glu Asn
    130                 135                 140
Gly Ile Cys Asn Ala Ile Leu Arg Cys Ser Val Glu Glu Gly Gly Glu
145                 150                 155                 160
Thr Ile Thr Tyr Glu Trp Thr Ser Met Gly Pro Gly Ala Ala Val Ser
                165                 170                 175
His Val Gly Leu His Asp Leu Asp Trp Ile Tyr Thr Cys Thr Ala Leu
            180                 185                 190
Asn Pro Val Ser Tyr Ser Asn Ser Thr Leu Thr Leu Ala Ala Gln Leu
        195                 200                 205
Cys Ala Ser Ser Lys Ala Ala Glu Gly Thr Tyr Cys Pro Val Lys Trp
    210                 215                 220
Ile Phe Leu Gly Asn Arg Leu Leu Leu Leu Val Phe Leu Gly Val Leu
225                 230                 235                 240
Arg Thr Trp His Ile Gln Ala Gln Val Leu Ser Lys Pro Leu Arg Pro
                245                 250                 255
Asn Ser Gly Glu Leu Val Asn Leu Ser Ser Ile Pro Tyr Pro Trp Glu
            260                 265                 270
Pro Ser His Thr Ala Asp Ala Thr Trp Leu Gly Lys Trp Gly Gly Ser
        275                 280                 285
Glu Gly Glu Arg Lys Ser Thr Trp Asn Ile Ser Thr Thr Lys Arg His
    290                 295                 300
```

Trp Lys Ser Phe Tyr Lys
305 310

<210> 49
<211> 841
<212> PRT
<213> *Homo sapiens*

<400> 49

```
Met Lys Leu Trp Ile His Leu Phe Tyr Ser Ser Leu Leu Ala Cys Ile
 1               5                  10                  15
Ser Leu His Ser Gln Thr Pro Val Leu Ser Ser Arg Gly Ser Cys Asp
            20                  25                  30
Ser Leu Cys Asn Cys Glu Glu Lys Asp Gly Thr Met Leu Ile Asn Cys
        35                  40                  45
Glu Ala Lys Gly Ile Lys Met Val Ser Glu Ile Ser Val Pro Pro Ser
    50                  55                  60
Arg Pro Phe Gln Leu Ser Leu Leu Asn Asn Gly Leu Thr Met Leu His
65                  70                  75                  80
Thr Asn Asp Phe Ser Gly Leu Thr Asn Ala Ile Ser Ile His Leu Gly
                85                  90                  95
Phe Asn Asn Ile Ala Asp Ile Glu Ile Gly Ala Phe Asn Gly Leu Gly
            100                 105                 110
Leu Leu Lys Gln Leu His Ile Asn His Asn Ser Leu Glu Ile Leu Lys
        115                 120                 125
Glu Asp Thr Phe His Gly Leu Glu Asn Leu Glu Phe Leu Gln Ala Asp
    130                 135                 140
Asn Asn Phe Ile Thr Val Ile Glu Pro Ser Ala Phe Ser Lys Leu Asn
145                 150                 155                 160
Arg Leu Lys Val Leu Ile Leu Asn Asp Asn Ala Ile Glu Ser Leu Pro
                165                 170                 175
Pro Asn Ile Phe Arg Phe Val Pro Leu Thr His Leu Asp Leu Arg Gly
            180                 185                 190
Asn Gln Leu Gln Thr Leu Pro Tyr Val Gly Phe Leu Glu His Ile Gly
        195                 200                 205
Arg Ile Leu Asp Leu Gln Leu Glu Asp Asn Lys Trp Ala Cys Asn Cys
    210                 215                 220
Asp Leu Leu Gln Leu Lys Thr Trp Leu Glu Asn Met Pro Pro Gln Ser
225                 230                 235                 240
Ile Ile Gly Asp Val Val Cys Asn Ser Pro Pro Phe Phe Lys Gly Ser
                245                 250                 255
Ile Leu Ser Arg Leu Lys Lys Glu Ser Ile Cys Pro Thr Pro Pro Val
            260                 265                 270
Tyr Glu Glu His Glu Asp Pro Ser Gly Ser Leu His Leu Ala Ala Thr
        275                 280                 285
Ser Ser Ile Asn Asp Ser Arg Met Ser Thr Lys Thr Thr Ser Ile Leu
    290                 295                 300
Lys Leu Pro Thr Lys Ala Pro Gly Leu Ile Pro Tyr Ile Thr Lys Pro
305                 310                 315                 320
Ser Thr Gln Leu Pro Gly Pro Tyr Cys Pro Ile Pro Cys Asn Cys Lys
                325                 330                 335
Val Leu Ser Pro Ser Gly Leu Leu Ile His Cys Gln Glu Arg Asn Ile
            340                 345                 350
Glu Ser Leu Ser Asp Leu Arg Pro Pro Pro Gln Asn Pro Arg Lys Leu
        355                 360                 365
Ile Leu Ala Gly Asn Ile Ile His Ser Leu Met Lys Ser Asp Leu Val
    370                 375                 380
Glu Tyr Phe Thr Leu Glu Met Leu His Leu Gly Asn Asn Arg Ile Glu
385                 390                 395                 400
```

Val Leu Glu Glu Gly Ser Phe Met Asn Leu Thr Arg Leu Gln Lys Leu
405 410 415
Tyr Leu Asn Gly Asn His Leu Thr Lys Leu Ser Lys Gly Met Phe Leu
420 425 430
Gly Leu His Asn Leu Glu Tyr Leu Tyr Leu Glu Tyr Asn Ala Ile Lys
435 440 445
Glu Ile Leu Pro Gly Thr Phe Asn Pro Met Pro Lys Leu Lys Val Leu
450 455 460
Tyr Leu Asn Asn Asn Leu Leu Gln Val Leu Pro Pro His Ile Phe Ser
465 470 475 480
Gly Val Pro Leu Thr Lys Val Asn Leu Lys Thr Asn Gln Phe Thr His
485 490 495
Leu Pro Val Ser Asn Ile Leu Asp Asp Leu Asp Leu Leu Thr Gln Ile
500 505 510
Asp Leu Glu Asp Asn Pro Trp Asp Cys Ser Cys Asp Leu Val Gly Leu
515 520 525
Gln Gln Trp Ile Gln Lys Leu Ser Lys Asn Thr Val Thr Asp Asp Ile
530 535 540
Leu Cys Thr Ser Pro Gly His Leu Asp Lys Lys Glu Leu Lys Ala Leu
545 550 555 560
Asn Ser Glu Ile Leu Cys Pro Gly Leu Val Asn Asn Pro Ser Met Pro
565 570 575
Thr Gln Thr Ser Tyr Leu Met Val Thr Thr Pro Ala Thr Thr Thr Asn
580 585 590
Thr Ala Asp Thr Ile Leu Arg Ser Leu Thr Asp Ala Val Pro Leu Ser
595 600 605
Val Leu Ile Leu Gly Leu Leu Ile Met Phe Ile Thr Ile Val Phe Cys
610 615 620
Ala Ala Gly Ile Val Val Leu Val Leu His Arg Arg Arg Arg Tyr Lys
625 630 635 640
Lys Lys Gln Val Asp Glu Gln Met Arg Asp Asn Ser Pro Val His Leu
645 650 655
Gln Tyr Ser Met Tyr Gly His Lys Thr Thr His His Thr Thr Glu Arg
660 665 670
Pro Ser Ala Ser Leu Tyr Glu Gln His Met Val Ser Pro Met Val His
675 680 685
Val Tyr Arg Ser Pro Ser Phe Gly Pro Lys His Leu Glu Glu Glu Glu
690 695 700
Glu Arg Asn Glu Lys Glu Gly Ser Asp Ala Lys His Leu Gln Arg Ser
705 710 715 720
Leu Leu Glu Gln Glu Asn His Ser Pro Leu Thr Gly Ser Asn Met Lys
725 730 735
Tyr Lys Thr Thr Asn Gln Ser Thr Glu Phe Leu Ser Phe Gln Asp Ala
740 745 750
Ser Ser Leu Tyr Arg Asn Ile Leu Glu Lys Glu Arg Glu Leu Gln Gln
755 760 765
Leu Gly Ile Thr Glu Tyr Leu Arg Lys Asn Ile Ala Gln Leu Gln Pro
770 775 780
Asp Met Glu Ala His Tyr Pro Gly Ala His Glu Glu Leu Lys Leu Met
785 790 795 800
Glu Thr Leu Met Tyr Ser Arg Pro Arg Lys Val Leu Val Glu Gln Thr
805 810 815
Lys Asn Glu Tyr Phe Glu Leu Lys Ala Asn Leu His Ala Glu Pro Asp
820 825 830
Tyr Leu Glu Val Leu Glu Gln Gln Thr
835 840

<210> 50
<211> 241

<212> PRT
<213> Homo sapiens

<400> 50

```
Met Gly Asn Pro Gly Leu Ala Trp Leu Val Leu Leu Gly Leu Val Leu
 1               5                  10                  15
Leu Leu Ser Ser Phe Met Glu Arg Gly Gly His Ser Pro Ser Pro Ala
            20                  25                  30
Ala Leu Ser Ala Met Glu Asn Leu Ile Thr Tyr Ala Val Gln Lys Gly
        35                  40                  45
His Leu Ser Ser Ser Tyr Val Gln Pro Leu Leu Val Lys Gly Glu Asn
    50                  55                  60
Cys Leu Ala Pro Arg Gln Lys Thr Ser Leu Lys Lys Ala Cys Pro Gly
65                  70                  75                  80
Val Val Pro Arg Ser Val Trp Gly Ala Arg Glu Thr His Cys Pro Arg
                85                  90                  95
Met Thr Leu Pro Ala Lys Tyr Gly Ile Ile Ile His Thr Ala Gly Arg
            100                 105                 110
Thr Cys Asn Ile Ser Asp Glu Cys Arg Leu Leu Val Arg Asp Ile Gln
        115                 120                 125
Ser Phe Tyr Ile Asp Arg Leu Lys Ser Cys Asp Ile Gly Tyr Asn Phe
    130                 135                 140
Leu Val Gly Gln Asp Gly Ala Ile Tyr Glu Gly Val Gly Trp Asn Val
145                 150                 155                 160
Gln Gly Ser Ser Thr Pro Gly Tyr Asp Asp Ile Ala Leu Gly Ile Thr
                165                 170                 175
Phe Met Gly Thr Phe Thr Gly Ile Pro Pro Asn Ala Ala Ala Leu Glu
            180                 185                 190
Ala Ala Gln Asp Leu Ile Gln Cys Ala Met Val Lys Gly Tyr Leu Thr
        195                 200                 205
Pro Asn Tyr Leu Leu Val Gly His Ser Asp Val Ala Arg Thr Leu Ser
    210                 215                 220
Pro Gly Gln Ala Leu Tyr Asn Ile Ile Ser Thr Trp Pro His Phe Lys
225                 230                 235                 240
His
```

<210> 51
<211> 369
<212> PRT
<213> *Homo sapiens*

<400> 51

```
Met Leu Pro Trp Leu Leu Val Phe Ser Ala Leu Gly Leu Gln Ala Trp
 1               5                  10                  15
Gly Asp Ser Ser Trp Asn Lys Thr Gln Ala Lys Gln Val Ser Glu Gly
            20                  25                  30
Leu Gln Tyr Leu Phe Glu Asn Ile Ser Gln Leu Thr Glu Lys Asp Val
        35                  40                  45
Ser Thr Thr Val Ser Arg Lys Ala Trp Gly Ala Glu Ala Val Gly Cys
    50                  55                  60
Ser Ile Gln Leu Thr Thr Pro Val Asn Val Leu Val Ile His His Val
65                  70                  75                  80
Pro Gly Leu Glu Cys His Asp Arg Thr Val Cys Ser Gln Arg Leu Arg
                85                  90                  95
Glu Leu Gln Ala His His Val His Asn Asn Ser Gly Cys Asp Val Ala
            100                 105                 110
Tyr Asn Phe Leu Val Gly Asp Asp Gly Arg Val Tyr Glu Gly Val Gly
        115                 120                 125
```

```
Trp Asn Ile Gln Gly Val His Thr Gln Gly Tyr Asn Asn Ile Ser Leu
    130                 135                 140
Gly Phe Ala Phe Phe Gly Thr Lys Lys Gly His Ser Pro Ser Pro Ala
145                 150                 155                 160
Ala Leu Ser Ala Met Glu Asn Leu Ile Thr Tyr Ala Val Gln Lys Gly
                165                 170                 175
His Leu Ser Ser Ser Tyr Val Gln Pro Leu Leu Val Lys Gly Glu Asn
            180                 185                 190
Cys Leu Ala Pro Arg Gln Lys Thr Ser Leu Lys Lys Ala Cys Pro Gly
        195                 200                 205
Val Val Pro Arg Ser Val Trp Gly Ala Arg Glu Thr His Cys Pro Arg
    210                 215                 220
Met Thr Leu Pro Ala Lys Tyr Gly Ile Ile Ile His Thr Ala Gly Arg
225                 230                 235                 240
Thr Cys Asn Ile Ser Asp Glu Cys Arg Leu Leu Val Arg Asp Ile Gln
                245                 250                 255
Ser Phe Tyr Ile Asp Arg Leu Lys Ser Cys Asp Ile Gly Tyr Asn Phe
            260                 265                 270
Leu Val Gly Gln Asp Gly Ala Ile Tyr Glu Gly Val Gly Trp Asn Val
        275                 280                 285
Gln Gly Ser Ser Thr Pro Gly Tyr Asp Asp Ile Ala Leu Gly Ile Thr
    290                 295                 300
Phe Met Gly Thr Phe Thr Gly Ile Pro Pro Asn Ala Ala Ala Leu Glu
305                 310                 315                 320
Ala Ala Gln Asp Leu Ile Gln Cys Ala Met Val Lys Gly Tyr Leu Thr
                325                 330                 335
Pro Asn Tyr Leu Leu Val Gly His Ser Asp Val Ala Arg Thr Leu Ser
            340                 345                 350
Pro Gly Gln Ala Leu Tyr Asn Ile Ile Ser Thr Trp Pro His Phe Lys
        355                 360                 365
His
```

<210> 52
<211> 382
<212> PRT
<213> Homo sapiens

<400> 52

```
Met Ala Pro Arg Ala Gly Gln Pro Gly Leu Gln Gly Leu Leu Leu Val
 1               5                  10                  15
Ala Ala Ala Leu Ser Gln Pro Ala Ala Pro Cys Pro Phe Gln Cys Tyr
            20                  25                  30
Cys Phe Gly Gly Pro Lys Leu Leu Leu Arg Cys Ala Ser Gly Ala Glu
        35                  40                  45
Leu Arg Gln Pro Pro Arg Asp Val Pro Pro Asp Ala Arg Asn Leu Thr
    50                  55                  60
Ile Val Gly Ala Asn Leu Thr Val Leu Arg Ala Ala Ala Phe Ala Gly
65                  70                  75                  80
Gly Asp Gly Asp Gly Asp Gln Ala Ala Gly Val Arg Leu Pro Leu Leu
                85                  90                  95
Ser Ala Leu Arg Leu Thr His Asn His Ile Glu Val Val Glu Asp Gly
            100                 105                 110
Ala Phe Asp Gly Leu Pro Ser Leu Ala Ala Leu Asp Leu Ser His Asn
        115                 120                 125
Pro Leu Arg Ala Leu Gly Gly Gly Ala Phe Arg Gly Leu Pro Ala Leu
    130                 135                 140
Arg Ser Leu Gln Leu Asn His Ala Leu Val Arg Gly Gly Pro Ala Leu
145                 150                 155                 160
```

```
Leu Ala Ala Leu Asp Ala Ala Leu Ala Pro Leu Ala Glu Leu Arg Leu
                165                 170                 175
Leu Gly Leu Ala Gly Asn Ala Leu Ser Arg Leu Pro Pro Ala Ala Leu
            180                 185                 190
Arg Leu Ala Arg Leu Glu Gln Leu Asp Val Arg Leu Asn Ala Leu Ala
        195                 200                 205
Gly Leu Asp Pro Asp Glu Leu Arg Ala Leu Glu Arg Asp Gly Gly Leu
    210                 215                 220
Pro Gly Pro Arg Leu Leu Leu Ala Asp Asn Pro Leu Arg Cys Gly Cys
225                 230                 235                 240
Ala Ala Arg Pro Leu Leu Ala Trp Leu Arg Asn Ala Thr Glu Arg Val
                245                 250                 255
Pro Asp Ser Arg Arg Leu Arg Cys Ala Ala Pro Arg Ala Leu Leu Asp
            260                 265                 270
Arg Pro Leu Leu Asp Leu Asp Gly Ala Arg Leu Arg Cys Ala Asp Ser
        275                 280                 285
Gly Ala Asp Ala Arg Gly Glu Glu Ala Glu Ala Ala Gly Pro Glu Leu
    290                 295                 300
Glu Ala Ser Tyr Val Phe Phe Gly Leu Val Leu Ala Leu Ile Gly Leu
305                 310                 315                 320
Ile Phe Leu Met Val Leu Tyr Leu Asn Arg Arg Gly Ile Gln Arg Trp
                325                 330                 335
Met Arg Asn Leu Arg Glu Ala Cys Arg Asp Gln Met Glu Gly Tyr His
            340                 345                 350
Tyr Arg Tyr Glu Gln Asp Ala Asp Pro Arg Arg Ala Pro Ala Pro Ala
        355                 360                 365
Ala Pro Ala Gly Ser Arg Ala Thr Ser Pro Gly Ser Gly Leu
    370                 375                 380
```

<210> 53
<211> 185
<212> PRT
<213> Homo sapiens

<400> 53

```
Met Met Leu Leu Leu Leu Cys Leu Gly Leu Thr Leu Val Cys Ala Gln
 1               5                  10                  15
Glu Glu Glu Asn Asn Asp Ala Val Thr Ser Asn Phe Asp Leu Ser Lys
            20                  25                  30
Ile Ser Gly Glu Trp Tyr Ser Val Leu Leu Ala Ser Asp Cys Arg Glu
        35                  40                  45
Lys Ile Glu Glu Asp Gly Ser Met Arg Val Phe Val Lys His Ile Asp
    50                  55                  60
Tyr Leu Gly Asn Ser Ser Leu Thr Phe Lys Leu His Glu Ile Glu Asn
65                  70                  75                  80
Gly Asn Cys Thr Glu Ile Asn Leu Ala Cys Lys Pro Thr Glu Lys Asn
                85                  90                  95
Ala Ile Cys Ser Thr Asp Tyr Asn Gly Leu Asn Val Ile Asp Ile Leu
            100                 105                 110
Glu Thr Asp Tyr Asp Asn Tyr Ile Tyr Phe Tyr Asn Lys Asn Ile Lys
        115                 120                 125
Asn Gly Glu Thr Phe Leu Met Leu Glu Leu Tyr Val Arg Thr Pro Asp
    130                 135                 140
Val Ser Ser Gln Leu Lys Glu Arg Phe Val Lys Tyr Cys Glu Glu His
145                 150                 155                 160
Gly Ile Asp Lys Glu Asn Ile Phe Asp Leu Thr Lys Val Asp Arg Cys
                165                 170                 175
Leu Gln Ala Arg Asp Glu Gly Ala Ala
            180                 185
```

<210> 54
<211> 586
<212> PRT
<213> Homo sapiens

<400> 54

```
Met His Tyr Asn Leu Gln Gly Pro Thr Arg Arg Ile Arg Ile Ser Leu
 1               5                  10                  15
Leu Asn Asp Gly Gly Leu Lys Ile Ala Asn Val Thr Lys Ala Asp Ala
            20                  25                  30
Gly Thr Tyr Thr Cys Met Ala Glu Asn Gln Phe Gly Lys Ala Asn Gly
        35                  40                  45
Thr Thr His Leu Val Val Thr Glu Pro Thr Arg Ile Thr Leu Ala Pro
    50                  55                  60
Ser Asn Met Asp Val Ser Val Gly Glu Ser Val Ile Leu Pro Cys Gln
65                  70                  75                  80
Val Gln His Asp Pro Leu Leu Asp Ile Ile Phe Thr Trp Tyr Phe Asn
                85                  90                  95
Gly Ala Leu Ala Asp Phe Lys Lys Asp Gly Ser His Phe Glu Lys Val
            100                 105                 110
Gly Gly Ser Ser Ser Gly Asp Leu Met Ile Arg Asn Ile Gln Leu Lys
        115                 120                 125
His Ser Gly Lys Tyr Val Cys Met Val Gln Thr Gly Val Asp Ser Val
    130                 135                 140
Ser Ser Ala Ala Asp Leu Ile Val Arg Gly Ser Pro Gly Pro Pro Glu
145                 150                 155                 160
Asn Val Lys Val Asp Glu Ile Thr Asp Thr Thr Ala Gln Leu Ser Trp
                165                 170                 175
Lys Glu Gly Lys Asp Asn His Ser Pro Val Ile Ser Tyr Ser Ile Gln
            180                 185                 190
Ala Arg Thr Pro Phe Ser Val Gly Trp Gln Thr Val Thr Thr Val Pro
        195                 200                 205
Glu Val Ile Asp Gly Lys Thr His Thr Ala Thr Val Val Glu Leu Asn
    210                 215                 220
Pro Trp Val Glu Tyr Glu Phe Arg Val Val Ala Ser Asn Lys Ile Gly
225                 230                 235                 240
Gly Gly Glu Pro Ser Leu Pro Ser Glu Lys Val Arg Thr Glu Glu Ala
                245                 250                 255
Val Pro Glu Val Pro Pro Ser Glu Val Asn Gly Gly Gly Gly Ser Arg
            260                 265                 270
Ser Glu Leu Val Ile Thr Trp Asp Pro Val Pro Glu Glu Leu Gln Asn
        275                 280                 285
Gly Glu Gly Phe Gly Tyr Val Val Ala Phe Arg Pro Leu Gly Val Thr
    290                 295                 300
Thr Trp Ile Gln Thr Val Val Thr Ser Pro Asp Thr Pro Arg Tyr Val
305                 310                 315                 320
Phe Arg Asn Glu Ser Ile Val Pro Tyr Ser Pro Tyr Glu Val Lys Val
                325                 330                 335
Gly Val Tyr Asn Asn Lys Gly Glu Gly Pro Phe Ser Pro Val Thr Thr
            340                 345                 350
Val Phe Ser Ala Glu Glu Glu Pro Thr Val Ala Pro Ser Gln Val Ser
        355                 360                 365
Ala Asn Ser Leu Ser Ser Ser Glu Ile Glu Val Ser Trp Asn Thr Ile
    370                 375                 380
Pro Trp Lys Leu Ser Asn Gly His Leu Leu Gly Tyr Glu Val Arg Tyr
385                 390                 395                 400
Trp Asn Gly Gly Gly Lys Glu Glu Ser Ser Ser Lys Met Lys Val Ala
                405                 410                 415
```

```
Gly Asn Glu Thr Ser Ala Arg Leu Arg Gly Leu Lys Ser Asn Leu Ala
            420                 425                 430
Tyr Tyr Thr Ala Val Arg Ala Tyr Asn Ser Ala Gly Ala Gly Pro Phe
        435                 440                 445
Ser Ala Thr Val Asn Val Thr Thr Lys Lys Thr Pro Pro Ser Gln Pro
    450                 455                 460
Pro Gly Asn Val Val Trp Asn Ala Thr Asp Thr Lys Val Leu Leu Asn
465                 470                 475                 480
Trp Glu Gln Val Lys Ala Met Glu Asn Glu Ser Glu Val Thr Gly Tyr
                485                 490                 495
Lys Val Phe Tyr Arg Thr Ser Ser Gln Asn Asn Val Gln Val Leu Asn
            500                 505                 510
Thr Asn Lys Thr Ser Ala Glu Leu Val Leu Pro Ile Lys Glu Asp Tyr
        515                 520                 525
Ile Ile Glu Val Lys Ala Thr Thr Asp Gly Gly Asp Gly Thr Ser Ser
    530                 535                 540
Glu Gln Ile Arg Ile Pro Arg Ile Thr Ser Met Asp Ala Arg Gly Ser
545                 550                 555                 560
Thr Ser Ala Ile Ser Asn Val His Pro Met Ser Ser Tyr Met Pro Ile
                565                 570                 575
Val Leu Phe Leu Ile Val Tyr Val Leu Trp
            580                 585
```

<210> 55
<211> 1026
<212> PRT
<213> Homo sapiens

<400> 55

```
Met Leu Val Val Glu Arg Val Met Val Leu Pro Ile Gly Phe Pro Leu
 1               5                  10                  15
Gly Val Ser Asp Asp Ser Thr Leu His Gly Pro Ile Phe Ile Gln Glu
            20                  25                  30
Pro Ser Pro Val Met Phe Pro Leu Asp Ser Glu Glu Lys Lys Val Lys
        35                  40                  45
Leu Asn Cys Glu Val Lys Gly Asn Pro Lys Pro His Ile Arg Trp Lys
    50                  55                  60
Leu Asn Gly Thr Asp Val Asp Thr Gly Met Asp Phe Arg Tyr Ser Val
65                  70                  75                  80
Val Glu Gly Ser Leu Leu Ile Asn Asn Pro Asn Lys Thr Gln Asp Ala
                85                  90                  95
Gly Thr Tyr Gln Cys Thr Ala Thr Asn Ser Phe Gly Thr Ile Val Ser
            100                 105                 110
Arg Glu Ala Lys Leu Gln Phe Ala Tyr Leu Asp Asn Phe Lys Thr Arg
        115                 120                 125
Thr Arg Ser Thr Val Ser Val Arg Arg Gly Gln Gly Met Val Leu Leu
    130                 135                 140
Cys Gly Pro Pro Pro His Ser Gly Glu Leu Ser Tyr Ala Trp Ile Phe
145                 150                 155                 160
Asn Glu Tyr Pro Ser Tyr Gln Asp Asn Arg Arg Phe Val Ser Gln Glu
                165                 170                 175
Thr Gly Asn Leu Tyr Ile Ala Lys Val Glu Lys Ser Asp Val Gly Asn
            180                 185                 190
Tyr Thr Cys Val Val Thr Asn Thr Val Thr Asn His Lys Val Leu Gly
        195                 200                 205
Pro Pro Thr Pro Leu Ile Leu Arg Asn Asp Gly Val Met Gly Glu Tyr
    210                 215                 220
Glu Pro Lys Ile Glu Val Gln Phe Pro Glu Thr Val Pro Thr Ala Lys
225                 230                 235                 240
```

```
Gly Ala Thr Val Lys Leu Glu Cys Phe Ala Leu Gly Asn Pro Val Pro
                245                 250                 255
Thr Ile Ile Trp Arg Arg Ala Asp Gly Lys Pro Ile Ala Arg Lys Ala
            260                 265                 270
Arg Arg His Lys Ser Asn Gly Ile Leu Glu Ile Pro Asn Phe Gln Gln
        275                 280                 285
Glu Asp Ala Gly Leu Tyr Glu Cys Val Ala Glu Asn Ser Arg Gly Lys
    290                 295                 300
Asn Val Ala Arg Gly Gln Leu Thr Phe Tyr Ala Gln Pro Asn Trp Ile
305                 310                 315                 320
Gln Lys Ile Asn Asp Ile His Val Ala Met Glu Glu Asn Val Phe Trp
                325                 330                 335
Glu Cys Lys Ala Asn Gly Arg Pro Lys Pro Thr Tyr Lys Trp Leu Lys
            340                 345                 350
Asn Gly Glu Pro Leu Leu Thr Arg Asp Arg Ile Gln Ile Glu Gln Gly
        355                 360                 365
Thr Leu Asn Ile Thr Ile Val Asn Leu Ser Asp Ala Gly Met Tyr Gln
    370                 375                 380
Cys Leu Ala Glu Asn Lys His Gly Val Ile Phe Ser Asn Ala Glu Leu
385                 390                 395                 400
Ser Val Ile Ala Val Gly Pro Asp Phe Ser Arg Thr Leu Leu Lys Arg
                405                 410                 415
Val Thr Leu Val Lys Val Gly Gly Glu Val Val Ile Glu Cys Lys Pro
            420                 425                 430
Lys Ala Ser Pro Lys Pro Val Tyr Thr Trp Lys Lys Gly Arg Asp Ile
        435                 440                 445
Leu Lys Glu Asn Glu Arg Ile Thr Ile Ser Glu Asp Gly Asn Leu Arg
    450                 455                 460
Ile Ile Asn Val Thr Lys Ser Asp Ala Gly Ser Tyr Thr Cys Ile Ala
465                 470                 475                 480
Thr Asn His Phe Gly Thr Ala Ser Ser Thr Gly Asn Leu Val Val Lys
                485                 490                 495
Asp Pro Thr Arg Val Met Val Pro Pro Ser Ser Met Asp Val Thr Val
            500                 505                 510
Gly Glu Ser Ile Val Leu Pro Cys Gln Val Thr His Asp His Ser Leu
        515                 520                 525
Asp Ile Val Phe Thr Trp Ser Phe Asn Gly His Leu Ile Asp Phe Asp
    530                 535                 540
Arg Asp Gly Asp His Phe Glu Arg Val Gly Gly Asp Ser Ala Gly Asp
545                 550                 555                 560
Leu Met Ile Arg Asn Ile Gln Leu Lys His Ala Gly Lys Tyr Val Cys
                565                 570                 575
Met Val Gln Thr Ser Val Asp Arg Leu Ser Ala Ala Ala Asp Leu Ile
            580                 585                 590
Val Arg Gly Pro Pro Gly Pro Pro Glu Ala Val Thr Ile Asp Glu Ile
        595                 600                 605
Thr Asp Thr Thr Ala Gln Leu Ser Trp Arg Pro Gly Pro Asp Asn His
    610                 615                 620
Ser Pro Ile Thr Met Tyr Val Ile Gln Ala Arg Thr Pro Phe Ser Val
625                 630                 635                 640
Gly Trp Gln Ala Val Ser Thr Val Pro Glu Leu Ile Asp Gly Lys Thr
                645                 650                 655
Phe Thr Ala Thr Val Val Gly Leu Asn Pro Trp Val Glu Tyr Glu Phe
            660                 665                 670
Arg Thr Val Ala Ala Asn Val Ile Gly Ile Gly Glu Pro Ser Arg Pro
        675                 680                 685
Ser Glu Lys Arg Arg Thr Glu Glu Ala Leu Pro Glu Val Thr Pro Ala
    690                 695                 700
Asn Val Ser Gly Gly Gly Gly Ser Lys Ser Glu Leu Val Ile Thr Trp
```

705 710 715 720
Glu Thr Val Pro Glu Glu Leu Gln Asn Gly Arg Gly Phe Gly Tyr Val
725 730 735
Val Ala Phe Arg Pro Tyr Gly Lys Met Ile Trp Met Leu Thr Val Leu
740 745 750
Ala Ser Ala Asp Ala Ser Arg Tyr Val Phe Arg Asn Glu Ser Val His
755 760 765
Pro Phe Ser Pro Phe Glu Val Lys Val Gly Val Phe Asn Asn Lys Gly
770 775 780
Glu Gly Pro Phe Ser Pro Thr Thr Val Val Tyr Ser Ala Glu Glu Glu
785 790 795 800
Pro Thr Lys Pro Pro Ala Ser Ile Phe Ala Arg Ser Leu Ser Ala Thr
805 810 815
Asp Ile Glu Val Phe Trp Ala Ser Pro Leu Glu Lys Asn Arg Gly Arg
820 825 830
Ile Gln Gly Tyr Glu Val Lys Tyr Trp Arg His Glu Asp Lys Glu Glu
835 840 845
Asn Ala Arg Lys Ile Arg Thr Val Gly Asn Gln Thr Ser Thr Lys Ile
850 855 860
Thr Asn Leu Lys Gly Ser Val Leu Tyr His Leu Ala Val Lys Ala Tyr
865 870 875 880
Asn Ser Ala Gly Thr Gly Pro Ser Ser Ala Thr Val Asn Val Thr Thr
885 890 895
Arg Lys Pro Pro Pro Ser Gln Pro Pro Gly Asn Ile Ile Trp Asn Ser
900 905 910
Ser Asp Ser Lys Ile Ile Leu Asn Trp Asp Gln Val Lys Ala Leu Asp
915 920 925
Asn Glu Ser Glu Val Lys Gly Tyr Lys Val Leu Tyr Arg Trp Asn Arg
930 935 940
Gln Ser Ser Thr Ser Val Ile Glu Thr Asn Lys Thr Ser Val Glu Leu
945 950 955 960
Ser Leu Pro Phe Asp Glu Asp Tyr Ile Ile Glu Ile Lys Pro Phe Ser
965 970 975
Asp Gly Gly Asp Gly Ser Ser Ser Glu Gln Ile Arg Ile Pro Lys Ile
980 985 990
Ser Asn Ala Tyr Ala Arg Gly Ser Gly Ala Ser Thr Ser Asn Ala Cys
995 1000 1005
Thr Leu Ser Ala Ile Ser Thr Ile Met Ile Ser Leu Thr Ala Arg Ser
1010 1015 1020
Ser Leu
1025

<210> 56
<211> 844
<212> PRT
<213> Homo sapiens

<400> 56
Met Asp Asn Pro Gln Ala Leu Pro Leu Phe Leu Leu Leu Ala Ser Leu
1 5 10 15
Val Gly Ile Leu Thr Leu Arg Ala Ser Ser Gly Leu Gln Gln Thr Asn
20 25 30
Phe Ser Ser Ala Phe Ser Ser Asp Ser Lys Ser Ser Ser Gln Gly Leu
35 40 45
Gly Val Glu Val Pro Ser Ile Lys Pro Pro Ser Trp Lys Val Pro Asp
50 55 60
Gln Phe Leu Asp Ser Lys Ala Ser Ala Gly Ile Ser Asp Ser Ser Trp
65 70 75 80
Phe Pro Glu Ala Leu Ser Ser Asn Met Ser Gly Ser Phe Trp Ser Asn

```
                85                  90                  95
Val Ser Ala Glu Gly Gln Asp Leu Ser Pro Val Ser Pro Phe Ser Glu
            100                 105                 110
Thr Pro Gly Ser Glu Val Phe Pro Asp Ile Ser Asp Pro Gln Val Pro
        115                 120                 125
Ala Lys Asp Pro Lys Pro Ser Phe Thr Val Lys Thr Pro Ala Ser Asn
    130                 135                 140
Ile Ser Thr Gln Val Ser His Thr Lys Leu Ser Val Glu Ala Pro Asp
145                 150                 155                 160
Ser Lys Phe Ser Pro Asp Asp Met Asp Leu Lys Leu Ser Ala Gln Ser
                165                 170                 175
Pro Glu Ser Lys Phe Ser Ala Glu Thr His Ser Ala Ala Ser Phe Pro
            180                 185                 190
Gln Gln Val Gly Gly Pro Leu Ala Val Leu Val Gly Thr Thr Ile Arg
        195                 200                 205
Leu Pro Leu Val Pro Ile Pro Asn Pro Gly Pro Pro Thr Ser Leu Val
    210                 215                 220
Val Trp Arg Arg Gly Ser Lys Val Leu Ala Ala Gly Gly Leu Gly Pro
225                 230                 235                 240
Gly Ala Pro Leu Ile Ser Leu Asp Pro Ala His Arg Asp His Leu Arg
                245                 250                 255
Phe Asp Gln Ala Arg Gly Val Leu Glu Leu Ala Ser Ala Gln Leu Asp
            260                 265                 270
Asp Ala Gly Val Tyr Thr Ala Glu Val Ile Arg Ala Gly Val Ser Gln
        275                 280                 285
Gln Thr His Glu Phe Thr Val Gly Val Tyr Glu Pro Leu Pro Gln Leu
    290                 295                 300
Ser Val Gln Pro Lys Ala Pro Glu Thr Glu Glu Gly Ala Ala Glu Leu
305                 310                 315                 320
Arg Leu Arg Cys Leu Gly Trp Gly Pro Gly Arg Gly Glu Leu Ser Trp
                325                 330                 335
Ser Arg Asp Gly Arg Ala Leu Glu Ala Ala Glu Ser Glu Gly Ala Glu
            340                 345                 350
Thr Pro Arg Met Arg Ser Glu Gly Asp Gln Leu Leu Ile Val Arg Pro
        355                 360                 365
Val Arg Ser Asp His Ala Arg Tyr Thr Cys Arg Val Arg Ser Pro Phe
    370                 375                 380
Gly His Arg Glu Ala Ala Ala Asp Val Ser Val Phe Tyr Gly Pro Asp
385                 390                 395                 400
Pro Pro Thr Ile Thr Val Ser Ser Asp Arg Asp Ala Ala Pro Ala Arg
                405                 410                 415
Phe Val Thr Ala Gly Ser Asn Val Thr Leu Arg Cys Ala Ala Ala Ser
            420                 425                 430
Arg Pro Pro Ala Asp Ile Thr Trp Ser Leu Ala Asp Pro Ala Glu Ala
        435                 440                 445
Ala Val Pro Ala Gly Ser Arg Leu Leu Leu Pro Ala Val Gly Pro Gly
    450                 455                 460
His Ala Gly Thr Tyr Ala Cys Leu Ala Ala Asn Pro Arg Thr Gly Arg
465                 470                 475                 480
Arg Arg Arg Ser Leu Leu Asn Leu Thr Val Ala Asp Leu Pro Pro Gly
                485                 490                 495
Ala Pro Gln Cys Ser Val Glu Gly Gly Pro Gly Asp Arg Ser Leu Arg
            500                 505                 510
Phe Arg Cys Ser Trp Pro Gly Gly Ala Pro Ala Ala Ser Leu Gln Phe
        515                 520                 525
Gln Gly Leu Pro Glu Gly Ile Arg Ala Gly Pro Val Ser Ser Val Leu
    530                 535                 540
Leu Ala Ala Val Pro Ala His Pro Arg Leu Ser Gly Val Pro Ile Thr
545                 550                 555                 560
```

```
Cys Leu Ala Arg His Leu Val Ala Thr Arg Thr Cys Thr Val Thr Pro
                565                 570                 575
Glu Ala Pro Arg Glu Val Leu Leu His Pro Leu Val Ala Glu Thr Arg
            580                 585                 590
Leu Gly Glu Ala Glu Val Ala Leu Glu Ala Ser Gly Cys Pro Pro Pro
        595                 600                 605
Ser Arg Ala Ser Trp Ala Arg Glu Gly Arg Pro Leu Ala Pro Gly Gly
    610                 615                 620
Gly Ser Arg Leu Arg Leu Ser Gln Asp Gly Arg Lys Leu His Ile Gly
625                 630                 635                 640
Asn Phe Ser Leu Asp Trp Asp Leu Gly Asn Tyr Ser Val Leu Cys Ser
                645                 650                 655
Gly Ala Leu Gly Ala Gly Gly Asp Gln Ile Thr Leu Ile Asp Gly Pro
            660                 665                 670
Ala Leu Gly Arg Thr Ser Thr Tyr Arg Asp Trp Val Ser Leu Leu Ile
        675                 680                 685
Leu Gly Pro Gln Glu Arg Ser Ala Val Val Pro Leu Pro Pro Arg Asn
    690                 695                 700
Pro Gly Thr Trp Thr Phe Arg Ile Leu Pro Ile Leu Gly Gly Gln Pro
705                 710                 715                 720
Gly Thr Pro Ser Gln Ser Arg Val Tyr Arg Ala Gly Pro Thr Leu Ser
                725                 730                 735
His Gly Ala Ile Ala Gly Ile Val Leu Gly Ser Leu Leu Gly Leu Ala
            740                 745                 750
Leu Leu Ala Val Leu Leu Leu Leu Cys Ile Cys Cys Leu Cys Arg Phe
        755                 760                 765
Arg Gly Lys Thr Pro Glu Lys Lys Lys His Pro Ser Thr Leu Val Pro
    770                 775                 780
Val Val Thr Pro Ser Glu Lys Lys Met His Ser Val Thr Pro Val Glu
785                 790                 795                 800
Ile Ser Trp Pro Leu Asp Leu Lys Val Pro Leu Glu Asp His Ser Ser
                805                 810                 815
Thr Arg Ala Tyr Gln Ala Thr Asp Pro Ser Ser Val Val Ser Val Gly
            820                 825                 830
Gly Gly Ser Lys Thr Val Arg Ala Ala Thr Gln Val
        835                 840
```

<210> 57
<211> 782
<212> PRT
<213> Homo sapiens

<400> 57

```
Met Asp Asn Pro Gln Ala Leu Pro Leu Phe Leu Leu Leu Ala Ser Leu
 1               5                  10                  15
Val Gly Ile Leu Thr Leu Arg Ala Ser Ser Gly Leu Gln Gln Thr Asn
            20                  25                  30
Phe Ser Ser Ala Phe Ser Ser Asp Ser Lys Ser Ser Ser Gln Gly Leu
        35                  40                  45
Gly Val Glu Val Pro Ser Ile Lys Pro Pro Ser Trp Lys Val Pro Asp
    50                  55                  60
Gln Phe Leu Asp Ser Lys Ala Ser Ala Gly Ile Ser Asp Ser Ser Trp
65                  70                  75                  80
Phe Pro Glu Ala Leu Ser Ser Asn Met Ser Gly Ser Phe Trp Ser Asn
                85                  90                  95
Val Ser Ala Glu Gly Gln Asp Leu Ser Pro Val Ser Pro Phe Ser Glu
            100                 105                 110
Thr Pro Gly Ser Glu Val Phe Pro Asp Ile Ser Asp Pro Gln Val Pro
        115                 120                 125
```

```
Ala Lys Asp Pro Lys Pro Ser Phe Thr Val Lys Thr Pro Ala Ser Asn
    130                 135                 140
Ile Ser Thr Gln Val Ser His Thr Lys Leu Ser Val Glu Ala Pro Asp
145                 150                 155                 160
Ser Lys Phe Ser Pro Asp Asp Met Asp Leu Lys Leu Ser Ala Gln Ser
                165                 170                 175
Pro Glu Ser Lys Phe Ser Ala Glu Thr His Ser Ala Ala Ser Phe Pro
            180                 185                 190
Gln Gln Val Gly Gly Pro Leu Ala Val Leu Val Gly Thr Thr Ile Arg
        195                 200                 205
Leu Pro Leu Val Pro Ile Pro Asn Pro Gly Pro Pro Thr Ser Leu Val
    210                 215                 220
Val Trp Arg Arg Gly Ser Lys Val Leu Ala Ala Gly Gly Leu Gly Pro
225                 230                 235                 240
Gly Ala Pro Leu Ile Ser Leu Asp Pro Ala His Arg Asp His Leu Arg
                245                 250                 255
Phe Asp Gln Ala Arg Gly Val Leu Glu Leu Ala Ser Ala Gln Leu Asp
            260                 265                 270
Asp Ala Gly Val Tyr Thr Ala Glu Val Ile Arg Ala Gly Val Ser Gln
        275                 280                 285
Gln Thr His Glu Phe Thr Val Gly Val Tyr Glu Pro Leu Pro Gln Leu
    290                 295                 300
Ser Val Gln Pro Lys Ala Pro Glu Thr Glu Glu Gly Ala Ala Glu Leu
305                 310                 315                 320
Arg Leu Arg Cys Leu Gly Trp Gly Pro Gly Arg Gly Glu Leu Ser Trp
                325                 330                 335
Ser Arg Asp Gly Arg Ala Leu Glu Ala Ala Glu Ser Glu Gly Ala Glu
            340                 345                 350
Thr Pro Arg Met Arg Ser Glu Gly Asp Gln Leu Leu Ile Val Arg Pro
        355                 360                 365
Val Arg Ser Asp His Ala Arg Tyr Thr Cys Arg Val Arg Ser Pro Phe
    370                 375                 380
Gly His Arg Glu Ala Ala Ala Asp Val Ser Val Phe Tyr Gly Pro Asp
385                 390                 395                 400
Pro Pro Thr Ile Thr Val Ser Ser Asp Arg Asp Ala Ala Pro Ala Arg
                405                 410                 415
Phe Val Thr Ala Gly Ser Asn Val Thr Leu Arg Cys Ala Ala Ala Ser
            420                 425                 430
Arg Pro Pro Ala Asp Ile Thr Trp Ser Leu Ala Asp Pro Ala Glu Ala
        435                 440                 445
Ala Val Pro Ala Gly Ser Arg Leu Leu Leu Pro Ala Val Gly Pro Gly
    450                 455                 460
His Ala Gly Thr Tyr Ala Cys Leu Ala Ala Asn Pro Arg Thr Gly Arg
465                 470                 475                 480
Arg Arg Arg Ser Leu Leu Asn Leu Thr Val Ala Asp Leu Pro Pro Gly
                485                 490                 495
Ala Pro Gln Cys Ser Val Glu Gly Gly Pro Gly Asp Arg Ser Leu Arg
            500                 505                 510
Phe Arg Cys Ser Trp Pro Gly Gly Ala Pro Ala Ala Ser Leu Gln Phe
        515                 520                 525
Gln Gly Leu Pro Glu Gly Ile Arg Ala Gly Pro Val Ser Ser Val Leu
    530                 535                 540
Leu Ala Ala Val Pro Ala His Pro Arg Leu Ser Gly Val Pro Ile Thr
545                 550                 555                 560
Cys Leu Ala Arg His Leu Val Ala Thr Arg Thr Cys Thr Val Thr Pro
                565                 570                 575
Glu Ala Pro Arg Glu Val Leu Leu His Pro Leu Val Ala Glu Thr Arg
            580                 585                 590
Leu Gly Glu Ala Glu Val Ala Leu Glu Ala Ser Gly Cys Pro Pro Pro
```

595 600 605
Ser Arg Ala Ser Trp Ala Arg Glu Gly Arg Pro Leu Ala Pro Gly Gly
610 615 620
Gly Ser Arg Leu Arg Leu Ser Gln Asp Gly Arg Lys Leu His Ile Gly
625 630 635 640
Asn Phe Ser Leu Asp Trp Asp Leu Gly Asn Tyr Ser Val Leu Cys Ser
645 650 655
Gly Ala Leu Gly Ala Gly Gly Asp Gln Ile Thr Leu Ile Gly Pro Thr
660 665 670
Leu Ser His Gly Ala Ile Ala Gly Ile Val Leu Gly Ser Leu Leu Gly
675 680 685
Leu Ala Leu Leu Ala Val Leu Leu Leu Leu Cys Ile Cys Cys Leu Cys
690 695 700
Arg Phe Arg Gly Lys Thr Pro Glu Lys Lys Lys His Pro Ser Thr Leu
705 710 715 720
Val Pro Val Val Thr Pro Ser Glu Lys Lys Met His Ser Val Thr Pro
725 730 735
Val Glu Ile Ser Trp Pro Leu Asp Leu Lys Val Pro Leu Glu Asp His
740 745 750
Ser Ser Thr Arg Ala Tyr Gln Ala Thr Asp Pro Ser Ser Val Val Ser
755 760 765
Val Gly Gly Gly Ser Lys Thr Val Arg Ala Ala Thr Gln Val
770 775 780

<210> 58
<211> 262
<212> PRT
<213> Homo sapiens

<400> 58
Met Asp Ser Leu Val Thr Ala Asn Thr Lys Phe Cys Phe Asp Leu Phe
1 5 10 15
Gln Glu Ile Gly Lys Asp Asp Arg His Lys Asn Ile Phe Phe Ser Pro
20 25 30
Leu Ser Leu Ser Ala Ala Leu Gly Met Val Arg Leu Gly Ala Arg Ser
35 40 45
Asp Ser Ala His Gln Ile Asp Glu Ala Gly Ser Leu Asn Asn Glu Ser
50 55 60
Gly Leu Val Ser Cys Tyr Phe Gly Gln Leu Leu Ser Lys Leu Asp Arg
65 70 75 80
Ile Lys Thr Asp Tyr Thr Leu Ser Ile Ala Asn Arg Leu Tyr Gly Glu
85 90 95
Gln Glu Phe Pro Ile Cys Gln Glu Tyr Leu Asp Gly Val Ile Gln Phe
100 105 110
Tyr His Thr Thr Ile Glu Ser Val Asp Phe Gln Lys Asn Pro Glu Lys
115 120 125
Ser Arg Gln Glu Ile Asn Phe Trp Val Glu Cys Gln Ser Gln Gly Lys
130 135 140
Ile Lys Glu Leu Phe Ser Lys Asp Ala Ile Asn Ala Glu Thr Val Leu
145 150 155 160
Val Leu Val Asn Ala Val Tyr Phe Lys Ala Lys Trp Glu Thr Tyr Phe
165 170 175
Asp His Glu Asn Thr Val Asp Ala Pro Phe Cys Leu Asn Ala Asn Glu
180 185 190
Asn Lys Ser Val Lys Met Met Thr Gln Lys Gly Leu Tyr Arg Ile Gly
195 200 205
Phe Ile Glu Glu Val Lys Ala Gln Ile Leu Glu Met Arg Tyr Thr Lys
210 215 220
Gly Lys Leu Ser Met Phe Val Leu Leu Pro Ser His Ser Lys Asp Asn

225 230 235 240
Leu Lys Gly Leu Glu Glu Val Asn Leu His Phe His Ile Ser Thr Lys
245 250 255
Tyr Leu Met Ile Asp Leu
260

<210> 59
<211> 394
<212> PRT
<213> Homo sapiens

<400> 59
Met Asp Ser Leu Val Thr Ala Asn Thr Lys Phe Cys Phe Asp Leu Phe
1 5 10 15
Gln Glu Ile Gly Lys Asp Asp Arg His Lys Asn Ile Phe Phe Ser Pro
20 25 30
Leu Ser Leu Ser Ala Ala Leu Gly Met Val Arg Leu Gly Ala Arg Ser
35 40 45
Asp Ser Ala His Gln Ile Asp Glu Val Leu His Phe Asn Lys Thr Thr
50 55 60
Glu Pro Leu Asp Gln Gln Ala Gly Ser Leu Asn Asn Glu Ser Gly Leu
65 70 75 80
Val Ser Cys Tyr Phe Gly Gln Leu Leu Ser Lys Leu Asp Arg Ile Lys
85 90 95
Thr Asp Tyr Thr Leu Ser Ile Ala Asn Arg Leu Tyr Gly Glu Gln Glu
100 105 110
Phe Pro Ile Cys Gln Glu Tyr Leu Asp Gly Val Ile Gln Phe Tyr His
115 120 125
Thr Thr Ile Glu Ser Val Asp Phe Gln Lys Asn Pro Glu Lys Ser Arg
130 135 140
Gln Glu Ile Asn Phe Trp Val Glu Cys Gln Ser Gln Gly Lys Ile Lys
145 150 155 160
Glu Leu Phe Ser Lys Asp Ala Ile Asn Ala Glu Thr Val Leu Val Leu
165 170 175
Val Asn Ala Val Tyr Phe Lys Ala Lys Trp Glu Thr Tyr Phe Asp His
180 185 190
Glu Asn Thr Val Asp Ala Pro Phe Cys Leu Asn Ala Asn Glu Asn Lys
195 200 205
Ser Val Lys Met Met Thr Gln Lys Gly Leu Tyr Arg Ile Gly Phe Ile
210 215 220
Glu Glu Val Lys Ala Gln Ile Leu Glu Met Arg Tyr Thr Lys Gly Lys
225 230 235 240
Leu Ser Met Phe Val Leu Leu Pro Ser His Ser Lys Asp Asn Leu Lys
245 250 255
Gly Leu Glu Glu Leu Glu Arg Lys Ile Thr Tyr Glu Lys Met Val Ala
260 265 270
Trp Ser Ser Ser Glu Asn Met Ser Glu Glu Ser Val Val Leu Ser Phe
275 280 285
Pro Arg Phe Thr Leu Glu Asp Ser Tyr Asp Leu Asn Ser Ile Leu Gln
290 295 300
Asp Met Gly Ile Thr Asp Ile Phe Asp Glu Thr Arg Ala Asp Leu Thr
305 310 315 320
Gly Ile Ser Pro Ser Pro Asn Leu Tyr Leu Ser Lys Ile Ile His Lys
325 330 335
Thr Phe Val Glu Val Asp Glu Asn Gly Thr Gln Ala Ala Ala Ala Thr
340 345 350
Gly Ala Val Val Ser Glu Arg Ser Leu Arg Ser Trp Val Glu Phe Asn
355 360 365
Ala Asn His Pro Phe Leu Phe Phe Ile Arg His Asn Lys Thr Gln Thr

370 375 380
Ile Leu Phe Tyr Gly Arg Val Cys Ser Pro
385 390

<210> 60
<211> 471
<212> PRT
<213> Homo sapiens

<400> 60
Met Ser Val Pro Leu Leu Lys Ile Gly Val Val Leu Ser Thr Met Ala
1 5 10 15
Met Ile Thr Asn Trp Met Ser Gln Thr Leu Pro Ser Leu Val Gly Leu
20 25 30
Asn Thr Thr Lys Leu Ser Ala Ala Gly Gly Gly Thr Leu Asp Arg Ser
35 40 45
Thr Gly Val Leu Pro Thr Asn Pro Glu Glu Ser Trp Gln Val Tyr Ser
50 55 60
Ser Ala Gln Asp Ser Glu Gly Arg Cys Ile Cys Thr Val Val Ala Pro
65 70 75 80
Gln Gln Thr Met Cys Ser Arg Asp Ala Arg Thr Lys Gln Leu Arg Gln
85 90 95
Leu Leu Glu Lys Val Gln Asn Met Ser Gln Ser Ile Glu Val Leu Asp
100 105 110
Arg Arg Thr Gln Arg Asp Leu Gln Tyr Val Glu Lys Met Glu Asn Gln
115 120 125
Met Lys Gly Leu Glu Ser Lys Phe Lys Gln Ala Ile Lys Ala Lys Met
130 135 140
Asp Glu Leu Arg Pro Leu Ile Pro Val Leu Glu Glu Tyr Lys Ala Asp
145 150 155 160
Ala Lys Leu Val Leu Gln Phe Lys Glu Glu Val Gln Asn Leu Thr Ser
165 170 175
Val Leu Asn Glu Leu Gln Glu Glu Ile Gly Ala Tyr Asp Tyr Asp Glu
180 185 190
Leu Gln Ser Arg Val Ser Asn Leu Glu Glu Arg Leu Arg Ala Cys Met
195 200 205
Gln Lys Leu Ala Cys Gly Lys Leu Thr Gly Ile Ser Asp Pro Val Thr
210 215 220
Val Lys Thr Ser Gly Ser Arg Phe Gly Ser Trp Met Thr Asp Pro Leu
225 230 235 240
Ala Pro Glu Gly Asp Asn Arg Val Trp Tyr Met Asp Gly Tyr His Asn
245 250 255
Asn Arg Phe Val Arg Glu Tyr Lys Ser Met Val Asp Phe Met Asn Thr
260 265 270
Asp Asn Phe Thr Ser His Arg Leu Pro His Pro Trp Ser Gly Thr Gly
275 280 285
Gln Val Val Tyr Asn Gly Ser Ile Tyr Phe Asn Lys Phe Gln Ser His
290 295 300
Ile Ile Ile Arg Phe Asp Leu Lys Thr Glu Thr Ile Leu Lys Thr Arg
305 310 315 320
Ser Leu Asp Tyr Ala Gly Tyr Asn Asn Met Tyr His Tyr Ala Trp Gly
325 330 335
Gly His Ser Asp Ile Asp Leu Met Val Asp Glu Ser Gly Leu Trp Ala
340 345 350
Val Tyr Ala Thr Asn Gln Asn Ala Gly Asn Ile Val Val Ser Arg Leu
355 360 365
Asp Pro Val Ser Leu Gln Thr Leu Gln Thr Trp Asn Thr Ser Tyr Pro
370 375 380
Lys Arg Ser Ala Gly Glu Ala Phe Ile Ile Cys Gly Thr Leu Tyr Val

385 390 395 400
Thr Asn Gly Tyr Ser Gly Gly Thr Lys Val His Tyr Ala Tyr Gln Thr
405 410 415
Asn Ala Ser Thr Tyr Glu Tyr Ile Asp Ile Pro Phe Gln Asn Lys Tyr
420 425 430
Ser His Ile Ser Met Leu Asp Tyr Asn Pro Lys Asp Arg Ala Leu Tyr
435 440 445
Ala Trp Asn Asn Gly His Gln Ile Leu Tyr Asn Val Thr Leu Phe His
450 455 460
Val Ile Arg Ser Asp Glu Leu
465 470

<210> 61
<211> 485
<212> PRT
<213> Homo sapiens

<400> 61
Met Ser Val Pro Leu Leu Lys Ile Gly Val Val Leu Ser Thr Met Ala
1 5 10 15
Met Ile Thr Asn Trp Met Ser Gln Thr Leu Pro Ser Leu Val Gly Leu
20 25 30
Asn Thr Thr Lys Leu Ser Ala Ala Gly Gly Gly Thr Leu Asp Arg Ser
35 40 45
Thr Gly Val Leu Pro Thr Asn Pro Glu Glu Ser Trp Gln Val Tyr Ser
50 55 60
Ser Ala Gln Asp Ser Glu Gly Arg Cys Ile Cys Thr Val Val Ala Pro
65 70 75 80
Gln Gln Thr Met Cys Ser Arg Asp Ala Arg Thr Lys Gln Leu Arg Gln
85 90 95
Leu Leu Glu Lys Val Gln Asn Met Ser Gln Ser Ile Glu Val Leu Asp
100 105 110
Arg Arg Thr Gln Arg Asp Leu Gln Tyr Val Glu Lys Met Glu Asn Gln
115 120 125
Met Lys Gly Leu Glu Ser Lys Phe Lys Gln Val Glu Glu Ile Ile Ser
130 135 140
Tyr Thr Trp Pro Arg Gln Phe Lys Ala Ile Lys Ala Lys Met Asp Glu
145 150 155 160
Leu Arg Pro Leu Ile Pro Val Leu Glu Glu Tyr Lys Ala Asp Ala Lys
165 170 175
Leu Val Leu Gln Phe Lys Glu Glu Val Gln Asn Leu Thr Ser Val Leu
180 185 190
Asn Glu Leu Gln Glu Glu Ile Gly Ala Tyr Asp Tyr Asp Glu Leu Gln
195 200 205
Ser Arg Val Ser Asn Leu Glu Glu Arg Leu Arg Ala Cys Met Gln Lys
210 215 220
Leu Ala Cys Gly Lys Leu Thr Gly Ile Ser Asp Pro Val Thr Val Lys
225 230 235 240
Thr Ser Gly Ser Arg Phe Gly Ser Trp Met Thr Asp Pro Leu Ala Pro
245 250 255
Glu Gly Asp Asn Arg Val Trp Tyr Met Asp Gly Tyr His Asn Asn Arg
260 265 270
Phe Val Arg Glu Tyr Lys Ser Met Val Asp Phe Met Asn Thr Asp Asn
275 280 285
Phe Thr Ser His Arg Leu Pro His Pro Trp Ser Gly Thr Gly Gln Val
290 295 300
Val Tyr Asn Gly Ser Ile Tyr Phe Asn Lys Phe Gln Ser His Ile Ile
305 310 315 320
Ile Arg Phe Asp Leu Lys Thr Glu Thr Ile Leu Lys Thr Arg Ser Leu

```
                325                 330                 335
Asp Tyr Ala Gly Tyr Asn Asn Met Tyr His Tyr Ala Trp Gly Gly His
            340                 345                 350
Ser Asp Ile Asp Leu Met Val Asp Glu Ser Gly Leu Trp Ala Val Tyr
        355                 360                 365
Ala Thr Asn Gln Asn Gly Asn Ile Val Val Ser Arg Leu Asp Pro
    370                 375                 380
Val Ser Leu Gln Thr Leu Gln Thr Trp Asn Thr Ser Tyr Pro Lys Arg
385                 390                 395                 400
Ser Ala Gly Glu Ala Phe Ile Ile Cys Gly Thr Leu Tyr Val Thr Asn
                405                 410                 415
Gly Tyr Ser Gly Gly Thr Lys Val His Tyr Ala Tyr Gln Thr Asn Ala
            420                 425                 430
Ser Thr Tyr Glu Tyr Ile Asp Ile Pro Phe Gln Asn Lys Tyr Ser His
        435                 440                 445
Ile Ser Met Leu Asp Tyr Asn Pro Lys Asp Arg Ala Leu Tyr Ala Trp
    450                 455                 460
Asn Asn Gly His Gln Ile Leu Tyr Asn Val Thr Leu Phe His Val Ile
465                 470                 475                 480
Arg Ser Asp Glu Leu
                485
```

<210> 62
<211> 286
<212> PRT
<213> Homo sapiens

<400> 62

```
Met Leu His Leu Leu Ala Leu Phe Leu His Cys Leu Pro Leu Ala Ser
 1                5                  10                  15
Gly Asp Tyr Asp Ile Cys Lys Ser Trp Val Thr Thr Asp Glu Gly Pro
            20                  25                  30
Thr Trp Glu Phe Tyr Ala Cys Gln Pro Lys Val Met Arg Leu Lys Asp
        35                  40                  45
Tyr Val Lys Val Lys Val Glu Pro Ser Gly Ile Thr Cys Gly Asp Pro
    50                  55                  60
Pro Glu Arg Phe Cys Ser His Glu Asn Pro Tyr Leu Cys Ser Asn Glu
65                  70                  75                  80
Cys Asp Ala Ser Asn Pro Asp Leu Ala His Pro Pro Arg Leu Met Phe
                85                  90                  95
Asp Lys Glu Glu Glu Gly Leu Ala Thr Tyr Trp Gln Ser Ile Thr Trp
            100                 105                 110
Ser Arg Tyr Pro Ser Pro Leu Glu Ala Asn Ile Thr Leu Ser Trp Asn
        115                 120                 125
Lys Thr Val Glu Leu Thr Asp Asp Val Val Met Thr Phe Glu Tyr Gly
    130                 135                 140
Arg Pro Thr Val Met Val Leu Glu Lys Ser Leu Asp Asn Gly Arg Thr
145                 150                 155                 160
Trp Gln Pro Tyr Gln Phe Tyr Ala Glu Asp Cys Met Glu Ala Phe Gly
                165                 170                 175
Met Ser Ala Arg Arg Ala Arg Asp Met Ser Ser Ser Ser Ala His Arg
            180                 185                 190
Val Leu Cys Thr Glu Glu Tyr Ser Arg Trp Ala Gly Ser Lys Lys Glu
        195                 200                 205
Lys His Val Arg Phe Glu Val Arg Asp Arg Phe Ala Ile Phe Ala Gly
    210                 215                 220
Pro Asp Leu Arg Asn Met Asp Asn Leu Tyr Thr Arg Leu Glu Ser Ala
225                 230                 235                 240
Lys Gly Leu Lys Glu Phe Phe Thr Leu Thr Asp Leu Arg Met Arg Leu
```

```
                245                 250                 255
Leu Arg Pro Ala Leu Gly Gly Thr Tyr Val Gln Arg Glu Asn Leu Tyr
            260                 265                 270
Lys Tyr Phe Tyr Ala Ile Ser Asn Ile Glu Val Ile Gly Arg
        275                 280                 285

      <210> 63
      <211> 533
      <212> PRT
      <213> Homo sapiens

      <400> 63
Met Leu His Leu Leu Ala Leu Phe Leu His Cys Leu Pro Leu Ala Ser
 1               5                  10                  15
Gly Asp Tyr Asp Ile Cys Lys Ser Trp Val Thr Thr Asp Glu Gly Pro
            20                  25                  30
Thr Trp Glu Phe Tyr Ala Cys Gln Pro Lys Val Met Arg Leu Lys Asp
        35                  40                  45
Tyr Val Lys Val Lys Val Glu Pro Ser Gly Ile Thr Cys Gly Asp Pro
    50                  55                  60
Pro Glu Arg Phe Cys Ser His Glu Asn Pro Tyr Leu Cys Ser Asn Glu
65                  70                  75                  80
Cys Asp Ala Ser Asn Pro Asp Leu Ala His Pro Pro Arg Leu Met Phe
                85                  90                  95
Asp Lys Glu Glu Glu Gly Leu Ala Thr Tyr Trp Gln Ser Ile Thr Trp
            100                 105                 110
Ser Arg Tyr Pro Ser Pro Leu Glu Ala Asn Ile Thr Leu Ser Trp Asn
        115                 120                 125
Lys Thr Val Glu Leu Thr Asp Asp Val Val Met Thr Phe Glu Tyr Gly
    130                 135                 140
Arg Pro Thr Val Met Val Leu Glu Lys Ser Leu Asp Asn Gly Arg Thr
145                 150                 155                 160
Trp Gln Pro Tyr Gln Phe Tyr Ala Glu Asp Cys Met Glu Ala Phe Gly
                165                 170                 175
Met Ser Ala Arg Arg Ala Arg Asp Met Ser Ser Ser Ser Ala His Arg
            180                 185                 190
Val Leu Cys Thr Glu Glu Tyr Ser Arg Trp Ala Gly Ser Lys Lys Glu
        195                 200                 205
Lys His Val Arg Phe Glu Val Arg Asp Arg Phe Ala Ile Phe Ala Gly
    210                 215                 220
Pro Asp Leu Arg Asn Met Asp Asn Leu Tyr Thr Arg Leu Glu Ser Ala
225                 230                 235                 240
Lys Gly Leu Lys Glu Phe Phe Thr Leu Thr Asp Leu Arg Met Arg Leu
                245                 250                 255
Leu Arg Pro Ala Leu Gly Gly Thr Tyr Val Gln Arg Glu Asn Leu Tyr
            260                 265                 270
Lys Tyr Phe Tyr Ala Ile Ser Asn Ile Glu Val Ile Gly Arg Cys Lys
        275                 280                 285
Cys Asn Leu His Ala Asn Leu Cys Ser Met Arg Glu Gly Ser Leu Gln
    290                 295                 300
Cys Glu Cys Glu His Asn Thr Thr Gly Pro Asp Cys Gly Lys Cys Lys
305                 310                 315                 320
Lys Asn Phe Arg Thr Arg Ser Trp Arg Ala Gly Ser Tyr Leu Pro Leu
                325                 330                 335
Pro His Gly Ser Pro Asn Ala Cys Thr Pro Pro Ser Pro Arg Glu Leu
            340                 345                 350
Gly Ala Asp Cys Glu Cys Tyr Gly His Ser Asn Arg Cys Ser Tyr Ile
        355                 360                 365
Asp Phe Leu Asn Val Val Thr Cys Val Ser Cys Lys His Asn Thr Arg
```

```
    370                 375                 380
Gly Gln His Cys Gln His Cys Arg Leu Gly Tyr Tyr Arg Asn Gly Ser
385                 390                 395                 400
Ala Glu Leu Asp Asp Glu Asn Val Cys Ile Glu Cys Asn Cys Asn Gln
                405                 410                 415
Ile Gly Ser Val His Asp Arg Cys Asn Glu Thr Gly Phe Cys Glu Cys
            420                 425                 430
Arg Glu Gly Ala Ala Gly Pro Lys Cys Asp Asp Cys Leu Pro Thr His
        435                 440                 445
Tyr Trp Arg Gln Gly Cys Tyr Pro Asn Val Cys Asp Asp Asp Gln Leu
    450                 455                 460
Leu Cys Gln Asn Gly Gly Thr Cys Leu Gln Asn Gln Arg Cys Ala Cys
465                 470                 475                 480
Pro Arg Gly Tyr Thr Gly Val Arg Cys Glu Gln Pro Arg Cys Asp Pro
                485                 490                 495
Ala Asp Asp Asp Gly Gly Leu Asp Cys Asp Arg Ala Pro Gly Ala Ala
            500                 505                 510
Pro Arg Pro Ala Thr Leu Leu Gly Cys Leu Leu Leu Leu Gly Leu Ala
        515                 520                 525
Ala Arg Leu Gly Arg
    530
```

<210> 64
<211> 495
<212> PRT
<213> Homo sapiens

<400> 64

```
Met Phe Ala Asn Ser Pro Gly Cys Ser Asn Met Leu His Tyr Val Tyr
 1                5                  10                  15
Cys Ala Cys Gly His Gly Leu Gln Leu Val Arg Ser Val Ser Ser Ser
            20                  25                  30
Val Asp Glu Gly Gly Thr Cys His Cys Met Val His Leu Pro Asn Asn
        35                  40                  45
Pro Ile Pro Leu Glu Gln Leu Glu Gln Leu Gln Ser Thr Ala Gln Glu
    50                  55                  60
Leu Ile Cys Lys Tyr Glu Gln Lys Leu Ser Arg Cys Ala Arg Ala Ile
65                  70                  75                  80
Glu Asp Lys Asp Asn Glu Val Leu Glu Met Ser His Met Leu Lys Ser
                85                  90                  95
Trp Asn Pro Ser Ala Leu Ala Ser Pro Tyr Glu Asn Pro Gly Phe Asn
            100                 105                 110
Leu Leu Cys Leu Glu Leu Glu Gly Ala Gln Glu Leu Val Thr Gln Leu
        115                 120                 125
Lys Ala Met Gly Gly Val Ser Val Ala Gly Asp Leu Leu His Gln Leu
    130                 135                 140
Gln Ser Gln Val Thr Asn Ala Ser Leu Thr Leu Lys Leu Leu Ala Asp
145                 150                 155                 160
Ser Asp Gln Cys Ser Phe Gly Ala Leu Gln Gln Glu Val Asp Val Leu
                165                 170                 175
Glu Ser Gln Leu Ser Glu Cys Glu Arg Glu Lys Glu Lys Glu Gly Leu
            180                 185                 190
Trp Thr Pro Trp Thr Thr Pro Pro Pro Ala Ser Cys Ala His Gly Gly
        195                 200                 205
Leu Gln Glu Val Ser Lys Ser Leu Val Val Gln Leu Thr Arg Arg Gly
    210                 215                 220
Phe Ser Tyr Lys Ala Gly Pro Trp Gly Arg Asp Ser Ala Pro Asn Pro
225                 230                 235                 240
Ala Ser Ser Leu Tyr Trp Val Ala Pro Leu Arg Thr Asp Gly Arg Tyr
```

```
                245                 250                 255
Phe Asp Tyr Tyr Arg Leu Pro Pro Ser Tyr Asn Asp Leu Ala Leu Met
            260                 265                 270
Lys Asn Tyr Glu Glu Arg Lys Met Gly Tyr Gly Asp Gly Ser Gly Asn
        275                 280                 285
Val Val Tyr Lys Asn Phe Met Tyr Phe Asn Tyr Cys Gly Thr Ser Asp
    290                 295                 300
Met Ala Lys Met Asp Leu Ser Ser Asn Thr Leu Val Leu Trp Arg Leu
305                 310                 315                 320
Leu Pro Gly Ala Thr Tyr Asn Asn Arg Phe Ser Cys Ala Gly Val Pro
                325                 330                 335
Trp Lys Asp Leu Asp Phe Ala Gly Asp Glu Lys Gly Leu Trp Val Leu
            340                 345                 350
Tyr Ala Thr Glu Glu Ser Lys Gly Asn Leu Val Val Ser Arg Leu Asn
        355                 360                 365
Ala Ser Thr Leu Glu Val Glu Lys Thr Trp Arg Thr Ser Gln Tyr Lys
    370                 375                 380
Pro Ala Leu Ser Gly Ala Phe Met Ala Cys Gly Val Leu Tyr Ala Leu
385                 390                 395                 400
His Ser Leu Asn Thr His Gln Glu Glu Ile Phe Tyr Ala Phe Asp Thr
                405                 410                 415
Thr Thr Gly Gln Glu Arg Arg Leu Ser Ile Leu Leu Asp Lys Met Leu
            420                 425                 430
Glu Lys Leu Gln Gly Ile Asn Tyr Cys Pro Ser Asp His Lys Pro Tyr
        435                 440                 445
Val Phe Ser Asp Gly Tyr Leu Ile Asn Tyr Asp Leu Thr Phe Leu Thr
    450                 455                 460
Met Lys Thr Arg Leu Pro Arg Pro Pro Thr Arg Arg Pro Ser Gly Ala
465                 470                 475                 480
His Ala Pro Pro Lys Pro Val Lys Pro Asn Glu Ala Ser Arg Pro
                485                 490                 495
```

<210> 65
<211> 350
<212> PRT
<213> Homo sapiens

<400> 65

```
Met Arg Asn His Lys Lys Val Thr Asn Ala Ser Leu Thr Leu Lys Leu
 1               5                  10                  15
Leu Ala Asp Ser Asp Gln Cys Ser Phe Gly Ala Leu Gln Gln Glu Val
            20                  25                  30
Asp Val Leu Glu Ser Gln Leu Ser Glu Ser Ser Cys Ala His Gly Gly
        35                  40                  45
Leu Gln Glu Val Ser Lys Ser Leu Val Val Gln Leu Thr Arg Arg Gly
    50                  55                  60
Phe Ser Tyr Lys Ala Gly Pro Trp Gly Arg Asp Ser Ala Pro Asn Pro
65                  70                  75                  80
Ala Ser Ser Leu Tyr Trp Val Ala Pro Leu Arg Thr Asp Gly Ser Tyr
                85                  90                  95
Gly Cys His Pro Ile Ile Leu Asn Ala Gly Thr Trp Pro Arg Tyr Phe
            100                 105                 110
Asp Tyr Tyr Arg Leu Cys Lys Ser Tyr Asn Asp Leu Ala Leu Leu Lys
        115                 120                 125
Asn Tyr Glu Glu Arg Lys Met Gly Tyr Gly Asp Gly Ser Gly Asn Val
    130                 135                 140
Val Tyr Lys Asn Phe Met Tyr Phe Asn Tyr Cys Gly Thr Ser Asp Met
145                 150                 155                 160
Ala Lys Met Asp Leu Ser Ser Asn Thr Leu Val Leu Trp Arg Leu Leu
```

```
                165                 170                 175
Pro Gly Ala Thr Tyr Asn Asn Arg Phe Ser Cys Ala Gly Val Pro Trp
            180                 185                 190
Lys Asp Leu Asp Phe Ala Gly Asp Glu Lys Gly Leu Trp Val Leu Tyr
        195                 200                 205
Ala Thr Glu Glu Ser Lys Gly Asn Leu Val Val Ser Arg Leu Asn Ala
    210                 215                 220
Ser Thr Leu Glu Val Glu Lys Thr Trp Arg Thr Ser Gln Tyr Lys Pro
225                 230                 235                 240
Ala Leu Ser Gly Ala Phe Met Ala Cys Gly Val Leu Tyr Ala Leu His
                245                 250                 255
Ser Leu Asn Thr His Gln Glu Glu Ile Phe Tyr Ala Phe Asp Thr Thr
            260                 265                 270
Thr Gly Gln Glu Arg Arg Leu Ser Ile Leu Leu Asp Lys Met Leu Glu
        275                 280                 285
Lys Leu Gln Gly Ile Asn Tyr Cys Pro Ser Asp His Lys Pro Tyr Val
    290                 295                 300
Phe Ser Asp Gly Tyr Leu Ile Asn Tyr Asp Leu Thr Phe Leu Thr Met
305                 310                 315                 320
Lys Thr Arg Leu Pro Arg Pro Pro Thr Arg Arg Pro Ser Gly Ala His
                325                 330                 335
Ala Pro Pro Lys Pro Val Lys Pro Asn Glu Ala Ser Arg Pro
            340                 345                 350
```

<210> 66
<211> 619
<212> PRT
<213> Homo sapiens

<400> 66

```
Met Gly Arg Gly Arg Ala Leu Leu Pro Ile Glu Met Leu Gln Leu Ser
 1                5                  10                  15
Leu Arg Glu Glu Ser Asp Thr Ala Arg Met Gly Ala Gln Glu Gln Ile
            20                  25                  30
Gly Leu Gln Asp Glu Ile Gln Ala Ala Asn Ala Gly Ile Ser Gly Ser
        35                  40                  45
Pro Gly Val Asp Gly Val Val Asp Gly Gly Ser Ser Arg Gly Asp Pro
    50                  55                  60
Ala Leu Thr Val Ser Val Cys Glu Val Pro Pro Val Arg Ser Pro Phe
65                  70                  75                  80
Arg Thr His Pro Gln Leu Pro Val Arg Leu Pro Arg Asn Leu Glu Phe
                85                  90                  95
Ser Val Pro Glu Arg Arg Thr Leu Arg Asn Arg Leu Thr Ser Ala Thr
            100                 105                 110
Leu Ala Pro Pro Thr Arg His Met Leu Leu Leu Leu Leu Leu Leu Pro
        115                 120                 125
Pro Leu Leu Cys Gly Arg Val Gly Ala Lys Glu Gln Lys Asp Tyr Leu
    130                 135                 140
Leu Thr Met Gln Lys Ser Val Thr Val Gln Glu Gly Leu Cys Val Ser
145                 150                 155                 160
Val Leu Cys Ser Phe Ser Tyr Pro Gln Asn Gly Trp Thr Ala Ser Asp
                165                 170                 175
Pro Val His Gly Tyr Trp Phe Arg Ala Gly Asp His Val Ser Arg Asn
            180                 185                 190
Ile Pro Val Ala Thr Asn Asn Pro Ala Arg Ala Val Gln Glu Glu Thr
        195                 200                 205
Arg Asp Arg Phe His Leu Leu Gly Asp Pro Gln Asn Lys Asp Cys Thr
    210                 215                 220
Leu Ser Ile Arg Asp Thr Arg Glu Ser Asp Ala Gly Thr Tyr Val Phe
```

```
225                 230                 235                 240
Cys Val Glu Arg Gly Asn Met Lys Trp Asn Tyr Lys Tyr Asp Gln Leu
                245                 250                 255
Ser Val Asn Val Thr Ala Leu Thr His Met Pro Thr Phe Ser Ile Pro
            260                 265                 270
Gly Thr Leu Glu Ser Gly His Pro Arg Asn Leu Thr Cys Ser Val Pro
        275                 280                 285
Trp Ala Cys Glu Gln Gly Thr Pro Pro Thr Ile Thr Trp Met Gly Ala
    290                 295                 300
Ser Val Ser Ser Leu Asp Pro Thr Ile Thr Arg Ser Ser Met Leu Ser
305                 310                 315                 320
Leu Ile Pro Gln Pro Gln Asp His Gly Thr Ser Leu Thr Cys Gln Val
                325                 330                 335
Thr Leu Pro Gly Ala Gly Val Thr Met Thr Arg Ala Val Arg Leu Asn
            340                 345                 350
Ile Ser Tyr Pro Pro Gln Asn Leu Thr Met Thr Val Phe Gln Gly Asp
        355                 360                 365
Gly Thr Ala Ser Thr Thr Leu Arg Asn Gly Ser Ala Leu Ser Val Leu
    370                 375                 380
Glu Gly Gln Ser Leu His Leu Val Cys Ala Val Asp Ser Asn Pro Pro
385                 390                 395                 400
Ala Arg Leu Ser Trp Thr Trp Gly Ser Leu Thr Leu Ser Pro Ser Gln
                405                 410                 415
Ser Ser Asn Leu Gly Val Leu Glu Leu Pro Arg Val His Val Lys Asp
            420                 425                 430
Glu Gly Glu Phe Thr Cys Arg Ala Gln Asn Pro Leu Gly Ser Gln His
        435                 440                 445
Ile Ser Leu Ser Leu Ser Leu Gln Asn Glu Tyr Thr Gly Lys Met Arg
    450                 455                 460
Pro Ile Ser Gly Val Thr Leu Gly Ala Phe Gly Gly Ala Gly Ala Thr
465                 470                 475                 480
Ala Leu Val Phe Leu Tyr Phe Cys Ile Ile Phe Val Val Val Arg Ser
                485                 490                 495
Cys Arg Lys Lys Ser Ala Arg Pro Ala Val Gly Val Gly Asp Thr Gly
            500                 505                 510
Met Glu Asp Ala Asn Ala Val Arg Gly Ser Ala Ser Gln Met Glu Glu
        515                 520                 525
Gly Thr Pro Gly Pro Pro Ser Trp Met Leu Ser Gly Ala Cys Trp Pro
    530                 535                 540
His Cys Ser Ala Leu Thr Pro Phe Ser Ser Ser Ile Gln Gly Pro Leu
545                 550                 555                 560
Ile Glu Ser Pro Ala Asp Asp Ser Pro Pro His His Ala Pro Pro Ala
                565                 570                 575
Leu Ala Thr Pro Ser Pro Glu Glu Gly Glu Ile Gln Tyr Ala Ser Leu
            580                 585                 590
Ser Phe His Lys Ala Arg Pro Gln Tyr Pro Gln Glu Gln Glu Ala Ile
        595                 600                 605
Gly Tyr Glu Tyr Ser Glu Ile Asn Ile Pro Lys
    610                 615
```

<210> 67
<211> 490
<212> PRT
<213> Homo sapiens

<400> 67

```
Met Leu Leu Leu Leu Leu Leu Leu Pro Pro Leu Leu Cys Gly Arg Val
 1                  5                  10                  15
Gly Ala Lys Glu Gln Lys Asp Tyr Leu Leu Thr Met Gln Lys Ser Val
```

```
            20                  25                  30
Thr Val Gln Glu Gly Leu Cys Val Ser Val Leu Cys Ser Phe Ser Tyr
        35                  40                  45
Pro Gln Asn Gly Trp Thr Ala Ser Asp Pro Val His Gly Tyr Trp Phe
    50                  55                  60
Arg Ala Gly Asp His Val Ser Arg Asn Ile Pro Val Ala Thr Asn Asn
65                  70                  75                  80
Pro Ala Arg Ala Val Gln Glu Glu Thr Arg Asp Arg Phe His Leu Leu
                85                  90                  95
Gly Asp Pro Gln Asn Lys Asp Cys Thr Leu Ser Ile Arg Asp Thr Arg
            100                 105                 110
Glu Ser Asp Ala Gly Thr Tyr Val Phe Cys Val Glu Arg Gly Asn Met
        115                 120                 125
Lys Trp Asn Tyr Lys Tyr Asp Gln Leu Ser Val Asn Val Thr Ala Leu
    130                 135                 140
Thr His Met Pro Thr Phe Ser Ile Pro Gly Thr Leu Glu Ser Gly His
145                 150                 155                 160
Pro Arg Asn Leu Thr Cys Ser Val Pro Trp Ala Cys Glu Gln Gly Thr
                165                 170                 175
Pro Pro Thr Ile Thr Trp Met Gly Ala Ser Val Ser Ser Leu Asp Pro
            180                 185                 190
Thr Ile Thr Arg Ser Ser Met Leu Ser Leu Ile Pro Gln Pro Gln Asp
        195                 200                 205
His Gly Thr Ser Leu Thr Cys Gln Val Thr Leu Pro Gly Ala Gly Val
    210                 215                 220
Thr Met Thr Arg Ala Val Arg Leu Asn Ile Ser Tyr Pro Pro Gln Asn
225                 230                 235                 240
Leu Thr Met Thr Val Phe Gln Gly Asp Gly Thr Ala Ser Thr Thr Leu
                245                 250                 255
Arg Asn Gly Ser Ala Leu Ser Val Leu Glu Gly Gln Ser Leu His Leu
            260                 265                 270
Val Cys Ala Val Asp Ser Asn Pro Pro Ala Arg Leu Ser Trp Thr Trp
        275                 280                 285
Gly Ser Leu Thr Leu Ser Pro Ser Gln Ser Ser Asn Leu Gly Val Leu
    290                 295                 300
Glu Leu Pro Arg Val His Val Lys Asp Glu Gly Glu Phe Thr Cys Arg
305                 310                 315                 320
Ala Gln Asn Pro Leu Gly Ser Gln His Ile Ser Leu Ser Leu Ser Leu
                325                 330                 335
Gln Asn Glu Tyr Thr Gly Lys Met Arg Pro Ile Ser Gly Val Thr Leu
            340                 345                 350
Gly Ala Phe Gly Gly Ala Gly Ala Thr Ala Leu Val Phe Leu Tyr Phe
        355                 360                 365
Cys Ile Ile Phe Val Val Val Arg Ser Cys Arg Lys Lys Ser Ala Arg
    370                 375                 380
Pro Ala Val Gly Val Gly Asp Thr Gly Met Glu Asp Ala Asn Ala Val
385                 390                 395                 400
Arg Gly Ser Ala Ser Gln Gly Pro Leu Thr Glu Ser Trp Lys Asp Gly
                405                 410                 415
Asn Pro Leu Lys Lys Pro Pro Pro Ala Val Ala Pro Ser Ser Gly Glu
            420                 425                 430
Glu Gly Glu Leu His Tyr Ala Thr Leu Ser Phe His Lys Val Lys Pro
        435                 440                 445
Gln Asp Pro Gln Gly Gln Glu Ala Thr Asp Ser Glu Tyr Ser Glu Ile
    450                 455                 460
Lys Ile His Lys Arg Glu Thr Ala Glu Thr Gln Ala Cys Leu Arg Asn
465                 470                 475                 480
His Asn Pro Ser Ser Lys Glu Val Arg Gly
                485                 490
```

<210> 68
<211> 462
<212> PRT
<213> Homo sapiens

<400> 68

```
Met Leu Pro Leu Trp Thr Leu Ser Leu Leu Leu Gly Ala Val Ala Gly
 1               5                  10                  15
Lys Glu Val Cys Tyr Glu Arg Leu Gly Cys Phe Ser Asp Asp Ser Pro
            20                  25                  30
Trp Ser Gly Ile Thr Glu Arg Pro Leu His Ile Leu Pro Trp Ser Pro
        35                  40                  45
Lys Asp Val Asn Thr Arg Phe Leu Leu Tyr Thr Asn Glu Asn Pro Asn
    50                  55                  60
Asn Phe Gln Glu Ile Ser Ala Val Asn Ser Ser Thr Ile Gln Ala Ser
65                  70                  75                  80
Tyr Phe Gly Thr Asp Lys Ile Thr Arg Ile Asn Ile Ala Gly Trp Lys
                85                  90                  95
Thr Asp Gly Lys Trp Gln Arg Asp Met Cys Asn Val Leu Leu Gln Leu
            100                 105                 110
Glu Asp Ile Asn Cys Ile Asn Leu Asp Trp Ile Asn Gly Ser Arg Glu
        115                 120                 125
Tyr Ile His Ala Val Asn Asn Leu Arg Val Val Gly Ala Glu Val Ala
    130                 135                 140
Tyr Phe Ile Asp Val Leu Met Lys Lys Phe Glu Tyr Ser Pro Ser Lys
145                 150                 155                 160
Val His Leu Ile Gly His Ser Leu Gly Ala His Leu Ala Gly Glu Ala
                165                 170                 175
Gly Ser Arg Ile Pro Gly Leu Gly Arg Ile Thr Gly Lys His Ala Leu
            180                 185                 190
Gln Leu Gly Leu Glu Cys Ala Thr Glu Gly Tyr Leu Leu Ser Ala Thr
        195                 200                 205
Leu Ala Asn Asn Val Asn Phe Val Asp Thr Asn His Met Asp Ala Thr
    210                 215                 220
Pro Ile Ile Pro Gln Trp Met Arg Gly Thr Ser Gly Thr Ser Asn Pro
225                 230                 235                 240
Leu Pro Val Thr Ser Ser Leu Cys Leu Trp Leu Ala Asp Leu Gly Ser
                245                 250                 255
Val Ser Leu Val Cys Leu Trp Pro Glu Met Ala Ser Phe Phe Asp Cys
            260                 265                 270
Asn His Ala Arg Ser Tyr Gln Phe Tyr Ala Glu Ser Ile Leu Asn Pro
        275                 280                 285
Asp Ala Phe Ile Ala Tyr Pro Cys Arg Ser Tyr Thr Ser Phe Lys Ala
    290                 295                 300
Gly Asn Cys Phe Phe Cys Ser Lys Glu Gly Cys Pro Thr Met Gly His
305                 310                 315                 320
Phe Ala Asp Arg Phe His Phe Lys Asn Met Lys Thr Asn Gly Ser His
                325                 330                 335
Tyr Phe Leu Asn Thr Gly Ser Leu Ser Pro Phe Ala Arg Trp Arg His
            340                 345                 350
Lys Leu Ser Val Lys Leu Ser Gly Ser Glu Val Thr Gln Gly Thr Val
        355                 360                 365
Phe Leu Arg Val Gly Gly Ala Val Arg Lys Thr Gly Glu Phe Ala Ile
    370                 375                 380
Val Ser Gly Lys Leu Glu Pro Gly Met Thr Tyr Thr Lys Leu Ile Asp
385                 390                 395                 400
Ala Asp Val Asn Val Gly Asn Ile Thr Ser Val Gln Phe Ile Trp Lys
                405                 410                 415
```

```
Lys His Leu Phe Glu Asp Ser Gln Asn Lys Leu Gly Ala Glu Met Val
            420                 425                 430
Ile Asn Thr Ser Gly Lys Tyr Gly Tyr Lys Ser Thr Phe Cys Ser Gln
        435                 440                 445
Asp Ile Met Gly Pro Asn Ile Leu Gln Asn Leu Lys Pro Cys
    450                 455                 460
```

<210> 69
<211> 255
<212> PRT
<213> Homo sapiens

<400> 69

```
Met Val Leu Leu Leu Val Ile Leu Ile Pro Val Leu Val Ser Ser Ala
 1               5                  10                  15
Gly Thr Ser Ala His Tyr Glu Met Leu Gly Thr Cys Arg Met Val Cys
            20                  25                  30
Asp Pro Tyr Gly Gly Thr Lys Ala Pro Ser Thr Ala Ala Thr Pro Asp
        35                  40                  45
Arg Gly Leu Met Gln Ser Leu Pro Thr Phe Ile Gln Gly Pro Lys Gly
    50                  55                  60
Glu Ala Gly Arg Pro Gly Lys Ala Gly Pro Arg Gly Pro Pro Gly Glu
65                  70                  75                  80
Pro Gly Pro Pro Gly Pro Met Gly Pro Pro Gly Glu Lys Gly Glu Pro
                85                  90                  95
Gly Arg Gln Gly Leu Pro Gly Pro Pro Gly Ala Pro Gly Leu Asn Ala
            100                 105                 110
Ala Gly Ala Ile Ser Ala Ala Thr Tyr Ser Thr Gly Pro Lys Ile Ala
        115                 120                 125
Phe Tyr Ala Gly Leu Lys Arg Gln His Glu Gly Tyr Glu Val Leu Lys
    130                 135                 140
Phe Asp Asp Val Val Thr Asn Leu Gly Asn His Tyr Asp Pro Thr Thr
145                 150                 155                 160
Gly Lys Phe Thr Cys Ser Ile Pro Gly Ile Tyr Phe Phe Thr Tyr His
                165                 170                 175
Val Leu Met Arg Gly Gly Asp Gly Thr Ser Met Trp Ala Asp Leu Cys
            180                 185                 190
Lys Asn Asn Gln Val Arg Ala Ser Ala Ile Ala Gln Asp Ala Asp Gln
        195                 200                 205
Asn Tyr Asp Tyr Ala Ser Asn Ser Val Val Leu His Leu Glu Pro Gly
    210                 215                 220
Asp Glu Val Tyr Ile Lys Leu Asp Gly Gly Lys Ala His Gly Gly Asn
225                 230                 235                 240
Asn Asn Lys Tyr Ser Thr Phe Ser Gly Phe Ile Ile Tyr Ala Asp
                245                 250                 255
```

<210> 70
<211> 784
<212> PRT
<213> Homo sapiens

<400> 70

```
Met Glu Gly Asp Gly Gly Thr Pro Trp Ala Leu Ala Leu Leu Arg Thr
 1               5                  10                  15
Phe Asp Ala Gly Glu Phe Thr Gly Trp Glu Lys Val Gly Ser Gly Gly
            20                  25                  30
Phe Gly Gln Val Tyr Lys Val Arg His Val His Trp Lys Thr Trp Leu
        35                  40                  45
Ala Ile Lys Cys Ser Pro Ser Leu His Val Asp Asp Arg Glu Arg Met
```

```
    50                  55                  60
Glu Leu Leu Glu Glu Ala Lys Lys Met Glu Met Ala Lys Phe Arg Tyr
65                  70                  75                  80
Ile Leu Pro Val Tyr Gly Ile Cys Arg Glu Pro Val Gly Leu Val Met
                85                  90                  95
Glu Tyr Met Glu Thr Gly Ser Leu Glu Lys Leu Leu Ala Ser Glu Pro
            100                 105                 110
Leu Pro Trp Asp Leu Arg Phe Arg Ile Ile His Glu Thr Ala Val Gly
        115                 120                 125
Met Asn Phe Leu His Cys Met Ala Pro Pro Leu Leu His Leu Asp Leu
    130                 135                 140
Lys Pro Ala Asn Ile Leu Leu Asp Ala His Tyr His Val Lys Ile Ser
145                 150                 155                 160
Asp Phe Gly Leu Ala Lys Cys Asn Gly Leu Ser His Ser His Asp Leu
                165                 170                 175
Ser Met Asp Gly Leu Phe Gly Thr Ile Ala Tyr Leu Pro Pro Glu Arg
            180                 185                 190
Ile Arg Glu Lys Ser Arg Leu Phe Asp Thr Lys His Asp Val Tyr Ser
        195                 200                 205
Phe Ala Ile Val Ile Trp Gly Val Leu Thr Gln Lys Lys Pro Phe Ala
    210                 215                 220
Asp Glu Lys Asn Ile Leu His Ile Met Val Lys Val Val Lys Gly His
225                 230                 235                 240
Arg Pro Glu Leu Pro Pro Val Cys Arg Ala Arg Pro Arg Ala Cys Ser
                245                 250                 255
His Leu Ile Arg Leu Met Gln Arg Cys Trp Gln Gly Asp Pro Arg Val
            260                 265                 270
Arg Pro Thr Phe Gln Glu Ile Thr Ser Glu Thr Glu Asp Leu Cys Glu
        275                 280                 285
Lys Pro Asp Asp Glu Val Lys Glu Thr Ala His Asp Leu Asp Val Lys
    290                 295                 300
Ser Pro Pro Glu Pro Arg Ser Glu Val Val Pro Ala Arg Leu Lys Arg
305                 310                 315                 320
Ala Ser Ala Pro Thr Phe Asp Asn Asp Tyr Ser Leu Ser Glu Leu Leu
                325                 330                 335
Ser Gln Leu Asp Ser Gly Val Ser Gln Ala Val Glu Gly Pro Glu Glu
            340                 345                 350
Leu Ser Arg Ser Ser Ser Glu Ser Lys Leu Pro Ser Ser Gly Ser Gly
        355                 360                 365
Lys Arg Leu Ser Gly Val Ser Ser Val Asp Ser Ala Phe Ser Ser Arg
    370                 375                 380
Gly Ser Leu Ser Leu Ser Phe Glu Arg Glu Pro Ser Thr Ser Asp Leu
385                 390                 395                 400
Gly Thr Thr Asp Val Gln Lys Lys Lys Leu Val Asp Ala Ile Val Ser
                405                 410                 415
Gly Asp Thr Ser Lys Leu Met Lys Ile Leu Gln Pro Gln Asp Val Asp
            420                 425                 430
Leu Ala Leu Asp Ser Gly Ala Ser Leu Leu His Leu Ala Val Glu Ala
        435                 440                 445
Gly Gln Glu Glu Cys Ala Lys Trp Leu Leu Leu Asn Asn Ala Asn Pro
    450                 455                 460
Asn Leu Ser Asn Arg Arg Gly Ser Thr Pro Leu His Met Ala Val Glu
465                 470                 475                 480
Arg Arg Val Arg Gly Val Val Glu Leu Leu Leu Ala Arg Lys Ile Ser
                485                 490                 495
Val Asn Ala Lys Asp Glu Asp Gln Trp Thr Ala Leu His Phe Ala Ala
            500                 505                 510
Gln Asn Gly Asp Glu Ser Ser Thr Arg Leu Leu Leu Glu Lys Asn Ala
        515                 520                 525
```

```
Ser Val Asn Glu Val Asp Phe Glu Gly Arg Thr Pro Met His Val Ala
    530                 535                 540
Cys Gln His Gly Gln Glu Asn Ile Val Arg Ile Leu Leu Arg Arg Gly
545                 550                 555                 560
Val Asp Val Ser Leu Gln Gly Lys Asp Ala Trp Leu Pro Leu His Tyr
                565                 570                 575
Ala Ala Trp Gln Gly His Leu Pro Ile Val Lys Leu Leu Ala Lys Gln
            580                 585                 590
Pro Gly Val Ser Val Asn Ala Gln Thr Leu Asp Gly Arg Thr Pro Leu
        595                 600                 605
His Leu Ala Ala Gln Arg Gly His Tyr Arg Val Ala Arg Ile Leu Ile
    610                 615                 620
Asp Leu Cys Ser Asp Val Asn Val Cys Ser Leu Leu Ala Gln Thr Pro
625                 630                 635                 640
Leu His Val Ala Ala Glu Thr Gly His Thr Ser Thr Ala Arg Leu Leu
                645                 650                 655
Leu His Arg Gly Ala Gly Lys Glu Ala Met Thr Ser Asp Gly Tyr Thr
            660                 665                 670
Ala Leu His Leu Ala Ala Arg Asn Gly His Leu Ala Thr Val Lys Leu
        675                 680                 685
Leu Val Glu Glu Lys Ala Asp Val Leu Ala Arg Gly Pro Leu Asn Gln
    690                 695                 700
Thr Ala Leu His Leu Ala Ala Ala His Gly His Ser Glu Val Val Glu
705                 710                 715                 720
Glu Leu Val Ser Ala Asp Val Ile Asp Leu Phe Asp Glu Gln Gly Leu
                725                 730                 735
Ser Ala Leu His Leu Ala Ala Gln Gly Arg His Ala Gln Thr Val Glu
            740                 745                 750
Thr Leu Leu Arg His Gly Ala His Ile Asn Leu Gln Ser Leu Lys Phe
        755                 760                 765
Gln Gly Gly His Gly Pro Ala Ala Thr Leu Leu Arg Arg Ser Lys Thr
    770                 775                 780
```

<210> 71
<211> 252
<212> PRT
<213> Homo sapiens

<400> 71

```
Met Ala Ala Pro Ala Leu Leu Leu Leu Ala Leu Leu Leu Pro Val Gly
 1                   5                  10                  15
Ala Trp Pro Gly Leu Pro Arg Arg Pro Cys Val His Cys Cys Arg Pro
            20                  25                  30
Ala Trp Pro Pro Gly Pro Tyr Ala Arg Val Ser Asp Arg Asp Leu Trp
        35                  40                  45
Arg Gly Asp Leu Trp Arg Gly Leu Pro Arg Val Arg Pro Thr Ile Asp
    50                  55                  60
Ile Glu Ile Leu Lys Gly Glu Lys Gly Glu Ala Gly Val Arg Gly Arg
65                  70                  75                  80
Ala Gly Arg Ser Gly Lys Glu Gly Pro Pro Gly Ala Arg Gly Leu Gln
                85                  90                  95
Gly Arg Arg Gly Gln Lys Gly Gln Val Gly Pro Pro Gly Ala Ala Cys
            100                 105                 110
Arg Arg Ala Tyr Ala Ala Phe Ser Val Gly Arg Arg Glu Gly Leu His
        115                 120                 125
Ser Ser Asp His Phe Gln Ala Val Pro Phe Asp Thr Glu Leu Val Asn
    130                 135                 140
Leu Asp Gly Ala Phe Asp Leu Ala Ala Gly Arg Phe Leu Cys Thr Val
145                 150                 155                 160
```

```
Pro Gly Val Tyr Phe Leu Ser Leu Asn Val His Thr Trp Asn Tyr Lys
                  165                 170                 175
Glu Thr Tyr Leu His Ile Met Leu Asn Arg Arg Pro Ala Ala Val Leu
              180                 185                 190
Tyr Ala Gln Pro Ser Glu Arg Ser Val Met Gln Ala Gln Ser Leu Met
          195                 200                 205
Leu Leu Leu Ala Ala Gly Asp Ala Val Trp Val Arg Met Phe Gln Arg
      210                 215                 220
Asp Arg Asp Asn Ala Ile Tyr Gly Glu His Gly Asp Leu Tyr Ile Thr
225                 230                 235                 240
Phe Ser Gly His Leu Val Lys Pro Ala Ala Glu Leu
                  245                 250
```

<210> 72
<211> 593
<212> PRT
<213> Homo sapiens

<400> 72

```
Met Pro Ser Ser Leu Phe Ala Asp Leu Glu Arg Asn Gly Ser Gly Gly
 1               5                  10                  15
Gly Gly Gly Gly Ser Ser Gly Gly Gly Glu Thr Leu Asp Asp Gln Arg
            20                  25                  30
Ala Leu Gln Leu Ala Leu Asp Gln Leu Ser Leu Leu Gly Leu Asp Ser
        35                  40                  45
Asp Glu Gly Ala Ser Leu Tyr Asp Ser Glu Pro Arg Lys Lys Ser Val
    50                  55                  60
Asn Met Thr Glu Cys Val Pro Val Pro Ser Ser Glu His Val Ala Glu
65                  70                  75                  80
Ile Val Gly Arg Gln Gly Arg Ser Arg Arg Asp Gly Glu Leu Asp Pro
                85                  90                  95
Ser Gly Ile Ser Pro Asp Asp Phe Ser Gly Ile Leu Gly Phe Gly Ser
            100                 105                 110
Gly Arg Leu Gln Ser Leu Gly Glu Gly Gln Ala Ala Asn Gly Leu Phe
        115                 120                 125
Leu Glu Arg Leu Ala Gly Gly Ile Arg Cys Pro Ala Arg Gly Ala Ala
    130                 135                 140
Arg Gly Cys Lys Ile Lys Ala Leu Arg Ala Lys Thr Asn Thr Tyr Ile
145                 150                 155                 160
Lys Thr Pro Val Arg Gly Glu Glu Pro Val Phe Val Val Thr Gly Arg
                165                 170                 175
Lys Glu Asp Val Ala Met Ala Arg Arg Glu Ile Ile Ser Ala Ala Glu
            180                 185                 190
His Phe Ser Met Ile Arg Ala Ser Arg Asn Lys Asn Thr Ala Leu Asn
        195                 200                 205
Gly Ala Val Pro Gly Pro Pro Asn Leu Pro Gly Gln Thr Thr Ile Gln
    210                 215                 220
Val Arg Val Pro Tyr Arg Val Val Gly Leu Val Val Gly Pro Lys Gly
225                 230                 235                 240
Ala Thr Ile Lys Arg Ile Gln Gln Gln Thr His Thr Tyr Ile Val Thr
                245                 250                 255
Pro Ser Arg Asp Lys Glu Pro Val Phe Glu Val Thr Gly Met Pro Glu
            260                 265                 270
Asn Val Asp Arg Ala Arg Glu Glu Ile Glu Ala His Ile Ala Leu Arg
        275                 280                 285
Thr Gly Gly Ile Ile Glu Leu Thr Asp Glu Asn Asp Phe His Ala Asn
    290                 295                 300
Gly Thr Asp Val Gly Phe Asp Leu His His Gly Ser Gly Gly Ala Ser
305                 310                 315                 320
```

```
Thr Asp Ser Tyr Phe Gly Gly Gly Thr Ser Ser Ser Ala Ala Ala Thr
                325                 330                 335
Gln Arg Leu Ala Asp Tyr Ser Pro Pro Ser Pro Ala Leu Ser Phe Ala
            340                 345                 350
His Asn Gly Asn Asn Asn Asn Asn Gly Asn Gly Tyr Thr Tyr Thr Ala
        355                 360                 365
Gly Gly Glu Ala Ser Val Pro Ser Pro Asp Gly Cys Pro Glu Leu Gln
    370                 375                 380
Pro Thr Phe Asp Pro Ala Pro Ala Pro Pro Pro Gly Ala Pro Leu Ile
385                 390                 395                 400
Trp Ala Gln Phe Glu Arg Ser Pro Gly Gly Gly Pro Ala Ala Pro Val
                405                 410                 415
Ser Ser Ser Cys Ser Ser Ser Ala Ser Ser Ser Ala Ser Ser Ser Ser
            420                 425                 430
Val Val Phe Pro Gly Gly Gly Ala Ser Ala Pro Ser Asn Ala Asn Leu
        435                 440                 445
Gly Leu Leu Val His Arg Arg Leu His Pro Gly Thr Ser Cys Pro Arg
    450                 455                 460
Leu Ser Pro Pro Leu His Met Ala Pro Gly Ala Gly Glu His His Leu
465                 470                 475                 480
Ala Arg Arg Val Arg Ser Asp Pro Gly Gly Gly Gly Leu Ala Tyr Ala
                485                 490                 495
Ala Tyr Ala Asn Gly Leu Gly Ala Gln Leu Pro Gly Leu Gln Pro Ser
            500                 505                 510
Asp Thr Ser Gly Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
        515                 520                 525
Ser Ser Ser Ser Gly Leu Arg Arg Lys Gly Ser Arg Asp Cys Ser Val
    530                 535                 540
Cys Phe Glu Ser Glu Val Ile Ala Ala Leu Val Pro Cys Gly His Asn
545                 550                 555                 560
Leu Phe Cys Met Glu Cys Ala Asn Arg Ile Cys Glu Lys Ser Glu Pro
                565                 570                 575
Glu Cys Pro Val Cys His Thr Ala Val Thr Gln Ala Ile Arg Ile Phe
            580                 585                 590
Ser
```

<210> 73
<211> 472
<212> PRT
<213> Homo sapiens

<400> 73

```
Met Pro Ser Ser Leu Phe Ala Asp Leu Glu Arg Asn Gly Ser Gly Gly
 1               5                  10                  15
Gly Gly Gly Gly Ser Ser Gly Gly Gly Glu Thr Leu Asp Asp Gln Arg
            20                  25                  30
Ala Leu Gln Leu Ala Leu Asp Gln Leu Ser Leu Leu Gly Leu Asp Ser
        35                  40                  45
Asp Glu Gly Ala Ser Leu Tyr Asp Ser Glu Pro Arg Lys Lys Ser Val
    50                  55                  60
Asn Met Thr Glu Cys Val Pro Val Pro Ser Ser Glu His Val Ala Glu
65                  70                  75                  80
Ile Val Gly Arg Gln Gly Cys Lys Ile Lys Ala Leu Arg Ala Lys Thr
                85                  90                  95
Asn Thr Tyr Ile Lys Thr Pro Val Arg Gly Glu Glu Pro Val Phe Val
            100                 105                 110
Val Thr Gly Arg Lys Glu Asp Val Ala Met Ala Arg Arg Glu Ile Ile
        115                 120                 125
```

```
Ser Ala Ala Glu His Phe Ser Met Ile Arg Ala Ser Arg Asn Lys Asn
    130                 135                 140
Thr Ala Leu Asn Gly Ala Val Pro Gly Pro Pro Asn Leu Pro Gly Gln
145                 150                 155                 160
Thr Thr Ile Gln Val Arg Val Pro Tyr Arg Val Val Gly Leu Val Val
                165                 170                 175
Gly Pro Lys Gly Ala Thr Ile Lys Arg Ile Gln Gln Gln Thr His Thr
            180                 185                 190
Tyr Ile Val Thr Pro Ser Arg Asp Lys Glu Pro Val Phe Glu Val Thr
        195                 200                 205
Gly Met Pro Glu Asn Val Asp Arg Ala Arg Glu Glu Ile Glu Ala His
    210                 215                 220
Ile Ala Leu Arg Thr Gly Gly Ile Ile Glu Leu Thr Asp Glu Asn Asp
225                 230                 235                 240
Phe His Ala Asn Gly Thr Asp Val Gly Phe Asp Leu His His Gly Ser
                245                 250                 255
Gly Gly Ser Gly Pro Gly Ser Leu Trp Ser Lys Pro Thr Pro Ser Ile
            260                 265                 270
Thr Pro Thr Pro Gly Arg Lys Pro Phe Ser Ser Tyr Arg Asn Asp Ser
        275                 280                 285
Ser Ser Ser Leu Gly Ser Ala Ser Thr Asp Ser Tyr Phe Gly Gly Gly
    290                 295                 300
Thr Ser Ser Ser Ala Ala Ala Thr Gln Arg Leu Ala Asp Tyr Ser Pro
305                 310                 315                 320
Ala Pro Ser Asn Ala Asn Leu Gly Leu Leu Val His Arg Arg Leu His
                325                 330                 335
Pro Gly Thr Ser Cys Pro Arg Leu Ser Pro Pro Leu His Met Ala Pro
            340                 345                 350
Gly Ala Gly Glu His His Leu Ala Arg Arg Val Arg Ser Asp Pro Gly
        355                 360                 365
Gly Gly Gly Leu Ala Tyr Ala Ala Tyr Ala Asn Gly Leu Gly Ala Gln
    370                 375                 380
Leu Pro Gly Leu Gln Pro Ser Asp Thr Ser Gly Ser Ser Ser Ser Ser
385                 390                 395                 400
Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Gly Leu Arg Arg Lys
                405                 410                 415
Gly Ser Arg Asp Cys Ser Val Cys Phe Glu Ser Glu Val Ile Ala Ala
            420                 425                 430
Leu Val Pro Cys Gly His Asn Leu Phe Cys Met Glu Cys Ala Asn Arg
        435                 440                 445
Ile Cys Glu Lys Ser Glu Pro Glu Cys Pro Val Cys His Thr Ala Val
    450                 455                 460
Thr Gln Ala Ile Arg Ile Phe Ser
465                 470
```

<210> 74
<211> 607
<212> PRT
<213> Homo sapiens

<400> 74

```
Met Trp Gly Leu Val Arg Leu Leu Leu Ala Trp Leu Gly Gly Trp Gly
 1               5                  10                  15
Cys Met Gly Arg Leu Ala Ala Pro Ala Arg Ala Trp Ala Gly Ser Arg
            20                  25                  30
Glu His Pro Gly Pro Ala Leu Leu Arg Thr Arg Arg Ser Trp Val Trp
        35                  40                  45
Asn Gln Phe Phe Val Ile Glu Glu Tyr Ala Gly Pro Glu Pro Val Leu
    50                  55                  60
```

```
Ile Gly Lys Leu His Ser Asp Val Asp Arg Gly Glu Gly Arg Thr Lys
65                  70                  75                  80
Tyr Leu Leu Thr Gly Glu Gly Ala Gly Thr Val Phe Val Ile Asp Glu
                85                  90                  95
Ala Thr Gly Asn Ile His Val Thr Lys Ser Leu Asp Arg Glu Glu Lys
            100                 105                 110
Ala Gln Tyr Val Leu Leu Ala Gln Ala Val Asp Arg Ala Ser Asn Arg
        115                 120                 125
Pro Leu Glu Pro Pro Ser Glu Phe Ile Ile Lys Val Gln Asp Ile Asn
    130                 135                 140
Asp Asn Pro Pro Ile Phe Pro Leu Gly Pro Tyr His Ala Thr Val Pro
145                 150                 155                 160
Glu Met Ser Asn Val Gly Thr Ser Val Ile Gln Val Thr Ala His Asp
                165                 170                 175
Ala Asp Asp Pro Ser Tyr Gly Asn Ser Ala Lys Leu Val Tyr Thr Val
            180                 185                 190
Leu Asp Gly Leu Pro Phe Phe Ser Val Asp Pro Gln Thr Gly Val Val
        195                 200                 205
Arg Thr Ala Ile Pro Asn Met Asp Arg Glu Thr Gln Glu Glu Phe Leu
    210                 215                 220
Val Val Ile Gln Ala Lys Asp Met Gly Gly His Met Gly Gly Leu Ser
225                 230                 235                 240
Gly Ser Thr Thr Val Thr Val Thr Leu Ser Asp Val Asn Asp Asn Pro
                245                 250                 255
Pro Lys Phe Pro Gln Ser Leu Tyr Gln Phe Ser Val Val Glu Thr Ala
            260                 265                 270
Gly Pro Gly Thr Leu Val Gly Arg Leu Arg Ala Gln Asp Pro Asp Leu
        275                 280                 285
Gly Asp Asn Ala Leu Met Ala Tyr Ser Ile Leu Asp Gly Glu Gly Ser
    290                 295                 300
Glu Ala Phe Ser Ile Ser Thr Asp Leu Gln Gly Arg Asp Gly Leu Leu
305                 310                 315                 320
Thr Val Arg Lys Pro Leu Asp Phe Glu Ser Gln Arg Ser Tyr Ser Phe
                325                 330                 335
Arg Val Glu Ala Thr Asn Thr Leu Ile Asp Pro Ala Tyr Leu Arg Arg
            340                 345                 350
Gly Pro Phe Lys Asp Val Ala Ser Val Arg Val Ala Val Gln Asp Ala
        355                 360                 365
Pro Glu Pro Pro Ala Phe Thr Gln Ala Ala Tyr His Leu Thr Val Pro
    370                 375                 380
Glu Asn Lys Ala Pro Gly Thr Leu Val Gly Gln Ile Ser Ala Ala Asp
385                 390                 395                 400
Leu Asp Ser Pro Ala Ser Pro Ile Arg Tyr Ser Ile Leu Pro His Ser
                405                 410                 415
Asp Pro Glu Arg Cys Phe Ser Ile Gln Pro Glu Glu Gly Thr Ile His
            420                 425                 430
Thr Ala Ala Pro Leu Asp Arg Glu Ala Arg Ala Trp His Asn Leu Thr
        435                 440                 445
Val Leu Ala Thr Glu Leu Val Pro Tyr Thr Pro Ala Tyr Ala Ser Gly
    450                 455                 460
Ala Pro Pro Pro Phe Cys Leu His Thr Ala Tyr Glu Asn Cys Pro Cys
465                 470                 475                 480
Ile Cys Gly Tyr Leu Asn Val Ser Val Lys Ala Tyr Met Asn Val His
                485                 490                 495
Met Trp Ala Met Val Leu Val Phe Ala Glu His Lys Gly Gly Gly Arg
            500                 505                 510
Gly Pro Gly Arg Gln Ala Val Asp Gly Gln Lys Gln Ser Thr Arg Trp
        515                 520                 525
Glu Leu Ser Gln Asn Cys Asn Tyr Leu Pro Lys Ser Arg Glu Gly Val
```

```
    530                 535                 540
His Pro Gly Thr Ser Met Arg Ala Gln Ala Ser Gln Leu Gln Gly Ser
545                 550                 555                 560
Arg Gly Thr His Arg Asn Cys Thr Arg Ile Ala Cys His Thr Arg Val
                565                 570                 575
Asn Pro Ile Leu Tyr His Ser Pro Thr Pro Gly His Arg Thr Thr Tyr
            580                 585                 590
Thr Cys Gly His Glu Tyr Ala Pro Ser Tyr Ala Glu Ser Asn Thr
        595                 600                 605
```

<210> 75
<211> 781
<212> PRT
<213> Homo sapiens

<400> 75

```
Met Trp Gly Leu Val Arg Leu Leu Leu Ala Trp Leu Gly Gly Trp Gly
 1               5                  10                  15
Cys Met Gly Arg Leu Ala Ala Pro Ala Arg Ala Trp Ala Gly Ser Arg
            20                  25                  30
Glu His Pro Gly Pro Ala Leu Leu Arg Thr Arg Arg Ser Trp Val Trp
        35                  40                  45
Asn Gln Phe Phe Val Ile Glu Glu Tyr Ala Gly Pro Glu Pro Val Leu
    50                  55                  60
Ile Gly Lys Leu His Ser Asp Val Asp Arg Gly Glu Gly Arg Thr Lys
65                  70                  75                  80
Tyr Leu Leu Thr Gly Glu Gly Ala Gly Thr Val Phe Val Ile Asp Glu
                85                  90                  95
Ala Thr Gly Asn Ile His Val Thr Lys Ser Leu Asp Arg Glu Glu Lys
            100                 105                 110
Ala Gln Tyr Val Leu Leu Ala Gln Ala Val Asp Arg Ala Ser Asn Arg
        115                 120                 125
Pro Leu Glu Pro Pro Ser Glu Phe Ile Ile Lys Val Gln Asp Ile Asn
    130                 135                 140
Asp Asn Pro Pro Ile Phe Pro Leu Gly Pro Tyr His Ala Thr Val Pro
145                 150                 155                 160
Glu Met Ser Asn Val Gly Thr Ser Val Ile Gln Val Thr Ala His Asp
                165                 170                 175
Ala Asp Asp Pro Ser Tyr Gly Asn Ser Ala Lys Leu Val Tyr Thr Val
            180                 185                 190
Leu Asp Gly Leu Pro Phe Phe Ser Val Asp Pro Gln Thr Gly Val Val
        195                 200                 205
Arg Thr Ala Ile Pro Asn Met Asp Arg Glu Thr Gln Glu Glu Phe Leu
    210                 215                 220
Val Val Ile Gln Ala Lys Asp Met Gly Gly His Met Gly Gly Leu Ser
225                 230                 235                 240
Gly Ser Thr Thr Val Thr Val Thr Leu Ser Asp Val Asn Asp Asn Pro
                245                 250                 255
Pro Lys Phe Pro Gln Ser Leu Tyr Gln Phe Ser Val Val Glu Thr Ala
            260                 265                 270
Gly Pro Gly Thr Leu Val Gly Arg Leu Arg Ala Gln Asp Pro Asp Leu
        275                 280                 285
Gly Asp Asn Ala Leu Met Ala Tyr Ser Ile Leu Asp Gly Glu Gly Ser
    290                 295                 300
Glu Ala Phe Ser Ile Ser Thr Asp Leu Gln Gly Arg Asp Gly Leu Leu
305                 310                 315                 320
Thr Val Arg Lys Pro Leu Asp Phe Glu Ser Gln Arg Ser Tyr Ser Phe
                325                 330                 335
Arg Val Glu Ala Thr Asn Thr Leu Ile Asp Pro Ala Tyr Leu Arg Arg
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            340                 345                 350
Gly Pro Phe Lys Asp Val Ala Ser Val Arg Val Ala Val Gln Asp Ala
        355                 360                 365
Pro Glu Pro Pro Ala Phe Thr Gln Ala Ala Tyr His Leu Thr Val Pro
    370                 375                 380
Glu Asn Lys Ala Pro Gly Thr Leu Val Gly Gln Ile Ser Ala Ala Asp
385                 390                 395                 400
Leu Asp Ser Pro Ala Ser Pro Ile Arg Tyr Ser Ile Leu Pro His Ser
                405                 410                 415
Asp Pro Glu Arg Cys Phe Ser Ile Gln Pro Glu Glu Gly Thr Ile His
            420                 425                 430
Thr Ala Ala Pro Leu Asp Arg Glu Ala Arg Ala Trp His Asn Leu Thr
        435                 440                 445
Val Leu Ala Thr Glu Leu Asp Ser Ser Ala Gln Ala Ser Arg Val Gln
    450                 455                 460
Val Ala Ile Gln Thr Leu Asp Glu Asn Asp Asn Ala Pro Gln Leu Ala
465                 470                 475                 480
Glu Pro Tyr Asp Thr Phe Val Cys Asp Ser Ala Ala Pro Gly Gln Leu
                485                 490                 495
Ile Gln Val Ile Arg Ala Leu Asp Arg Asp Glu Val Gly Asn Ser Ser
            500                 505                 510
His Val Ser Phe Gln Gly Pro Leu Gly Pro Asp Ala Asn Phe Thr Val
        515                 520                 525
Gln Asp Asn Arg Asp Gly Ser Ala Ser Leu Leu Leu Pro Ser Arg Pro
    530                 535                 540
Ala Pro Pro Arg His Ala Pro Tyr Leu Val Pro Ile Glu Leu Trp Asp
545                 550                 555                 560
Trp Gly Gln Pro Ala Leu Ser Ser Thr Ala Thr Val Thr Val Ser Val
                565                 570                 575
Cys Arg Cys Gln Pro Asp Gly Ser Val Ala Ser Cys Trp Pro Glu Ala
            580                 585                 590
His Leu Ser Ala Ala Gly Leu Ser Thr Gly Ala Leu Leu Ala Ile Ile
        595                 600                 605
Thr Cys Val Gly Ala Leu Leu Ala Leu Val Val Leu Phe Val Ala Leu
    610                 615                 620
Arg Arg Gln Lys Gln Glu Ala Leu Met Val Leu Glu Glu Glu Asp Val
625                 630                 635                 640
Arg Glu Asn Ile Ile Thr Tyr Asp Asp Glu Gly Gly Gly Glu Glu Asp
                645                 650                 655
Thr Glu Ala Phe Asp Ile Thr Ala Leu Gln Asn Pro Asp Gly Ala Ala
            660                 665                 670
Pro Pro Ala Pro Gly Pro Pro Ala Arg Arg Asp Val Leu Pro Arg Ala
        675                 680                 685
Arg Val Ser Arg Gln Pro Arg Pro Pro Gly Pro Ala Asp Val Ala Gln
    690                 695                 700
Leu Leu Ala Leu Arg Leu Arg Glu Ala Asp Glu Asp Pro Gly Val Pro
705                 710                 715                 720
Pro Tyr Asp Ser Val Gln Val Tyr Gly Tyr Glu Gly Arg Gly Ser Ser
                725                 730                 735
Cys Gly Ser Leu Ser Ser Leu Gly Ser Gly Ser Glu Ala Gly Gly Ala
            740                 745                 750
Pro Gly Pro Ala Glu Pro Leu Asp Asp Trp Gly Pro Leu Phe Arg Thr
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Leu Ala Glu Leu Tyr Gly Ala Lys Glu Pro Pro Ala Pro
    770                 775                 780
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<210> 76
<211> 640
<212> PRT

<213> Homo sapiens

<400> 76

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 1               5                  10                  15
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            20                  25                  30
Ser Cys Leu Arg Leu Val Tyr Gln Ile Thr Thr Ser Ser Glu Ser Leu
        35                  40                  45
Ser Asp Pro Ser Gln Leu Asn Leu Tyr Met Arg Phe Glu Asp Glu Ser
    50                  55                  60
Phe Asp Arg Leu Leu Trp Ser Ala Lys Glu Pro Ser Asp Ser Trp Leu
65                  70                  75                  80
Ile Ala Ser Leu Asp Leu Gln Asn Ser Ser Lys Lys Phe Lys Ile Leu
                85                  90                  95
Ile Glu Gly Val Leu Gly Gln Gly Asn Thr Ala Ser Ile Ala Leu Phe
            100                 105                 110
Glu Ile Lys Met Thr Thr Gly Tyr Cys Ile Glu Cys Asp Phe Glu Glu
        115                 120                 125
Asn His Leu Cys Gly Phe Val Asn Arg Trp Asn Pro Asn Val Asn Trp
    130                 135                 140
Phe Val Gly Gly Gly Ser Ile Arg Asn Val His Ser Ile Leu Pro Gln
145                 150                 155                 160
Asp His Thr Phe Lys Ser Glu Leu Gly His Tyr Met Tyr Val Asp Ser
                165                 170                 175
Val Tyr Val Lys His Phe Gln Glu Val Ala Gln Leu Ile Ser Pro Leu
            180                 185                 190
Thr Thr Ala Pro Met Ala Gly Cys Leu Ser Phe Tyr Tyr Gln Ile Gln
        195                 200                 205
Gln Gly Asn Asp Asn Val Phe Ser Leu Tyr Thr Arg Asp Val Ala Gly
    210                 215                 220
Leu Tyr Glu Glu Ile Trp Lys Ala Asp Arg Pro Gly Asn Ala Ala Trp
225                 230                 235                 240
Asn Leu Ala Glu Val Glu Phe Thr Cys His Phe Pro Leu Gln Val Ile
                245                 250                 255
Phe Glu Val Ala Phe Asn Gly Pro Lys Gly Gly Tyr Val Ala Leu Asp
            260                 265                 270
Asp Ile Ser Phe Ser Pro Val His Cys Gln Asn Gln Thr Glu Leu Leu
        275                 280                 285
Phe Ser Ala Val Glu Ala Ser Cys Asn Phe Glu Gln Asp Leu Cys Asn
    290                 295                 300
Phe Tyr Gln Asp Lys Glu Gly Pro Gly Trp Thr Arg Val Lys Val Lys
305                 310                 315                 320
Pro Asn Met Tyr Arg Ala Gly Asp His Thr Thr Gly Leu Gly Tyr Tyr
                325                 330                 335
Leu Leu Ala Asn Thr Lys Phe Thr Ser Gln Pro Gly Tyr Ile Gly Arg
            340                 345                 350
Leu Tyr Gly Pro Ser Leu Pro Gly Asn Leu Gln Tyr Cys Leu Arg Phe
        355                 360                 365
His Tyr Ala Ile Tyr Gly Phe Leu Lys Met Ser Asp Thr Leu Ala Val
    370                 375                 380
Tyr Ile Phe Glu Glu Asn His Val Val Gln Glu Lys Ile Trp Ser Val
385                 390                 395                 400
Leu Glu Ser Pro Arg Gly Val Trp Met Gln Ala Glu Ile Thr Phe Lys
                405                 410                 415
Lys Pro Met Pro Thr Lys Val Val Phe Met Ser Leu Cys Lys Ser Phe
            420                 425                 430
Trp Asp Cys Gly Leu Val Ala Leu Asp Asp Ile Thr Ile Gln Leu Gly
        435                 440                 445
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Ser Cys Ser Ser Ser Glu Lys Leu Pro Pro Pro Pro Gly Glu Cys Thr
    450                 455                 460
Phe Glu Gln Asp Glu Cys Thr Phe Thr Gln Glu Lys Arg Asn Arg Ser
465                 470                 475                 480
Ser Trp His Arg Arg Arg Gly Glu Thr Pro Thr Ser Tyr Thr Gly Pro
                485                 490                 495
Lys Gly Asp His Thr Thr Gly Val Gly Tyr Tyr Met Tyr Ile Glu Ala
            500                 505                 510
Ser His Met Val Tyr Gly Gln Lys Ala Arg Leu Leu Ser Arg Pro Leu
        515                 520                 525
Arg Gly Val Ser Gly Lys His Cys Leu Thr Phe Phe Tyr His Met Tyr
    530                 535                 540
Gly Gly Gly Thr Gly Leu Leu Ser Val Tyr Leu Lys Lys Glu Glu Asp
545                 550                 555                 560
Ser Glu Glu Ser Leu Leu Trp Arg Arg Arg Gly Glu Gln Ser Ile Ser
                565                 570                 575
Trp Leu Arg Ala Leu Ile Glu Tyr Ser Cys Glu Arg Gln His Gln Ile
            580                 585                 590
Ile Phe Glu Ala Ile Arg Gly Val Ser Ile Arg Ser Asp Ile Ala Ile
        595                 600                 605
Asp Asp Val Lys Phe Gln Ala Gly Pro Cys Gly Glu Met Glu Asp Thr
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<210> 77
<211> 686
<212> PRT
<213> Homo sapiens

<400> 77

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            20                  25                  30
Cys Gly Phe Asp Ser Val Leu Ala Ser Leu Pro Trp Ile Leu Asn Glu
        35                  40                  45
Glu Gly His Tyr Ile Tyr Val Asp Thr Ser Phe Gly Lys Gln Gly Glu
    50                  55                  60
Lys Ala Val Leu Leu Ser Pro Asp Leu Gln Ala Glu Glu Trp Ser Cys
65                  70                  75                  80
Leu Arg Leu Val Tyr Gln Ile Thr Thr Ser Ser Glu Ser Leu Ser Asp
                85                  90                  95
Pro Ser Gln Leu Asn Leu Tyr Met Arg Phe Glu Asp Glu Ser Phe Asp
            100                 105                 110
Arg Leu Leu Trp Ser Ala Lys Glu Pro Ser Asp Ser Trp Leu Ile Ala
        115                 120                 125
Ser Leu Asp Leu Gln Asn Ser Ser Lys Lys Phe Lys Ile Leu Ile Glu
    130                 135                 140
Gly Val Leu Gly Gln Gly Asn Thr Ala Ser Ile Ala Leu Phe Glu Ile
145                 150                 155                 160
Lys Met Thr Thr Gly Tyr Cys Ile Glu Cys Asp Phe Glu Glu Asn His
                165                 170                 175
Leu Cys Gly Phe Val Asn Arg Trp Asn Pro Asn Val Asn Trp Phe Val
            180                 185                 190
Gly Gly Gly Ser Ile Arg Asn Val His Ser Ile Leu Pro Gln Asp His
        195                 200                 205
Thr Phe Lys Ser Glu Leu Gly His Tyr Met Tyr Val Asp Ser Val Tyr
    210                 215                 220
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Val Lys His Phe Gln Glu Val Ala Gln Leu Ile Ser Pro Leu Thr Thr
225                 230                 235                 240
Ala Pro Met Ala Gly Cys Leu Ser Phe Tyr Tyr Gln Ile Gln Gln Gly
                245                 250                 255
Asn Asp Asn Val Phe Ser Leu Tyr Thr Arg Asp Val Ala Gly Leu Tyr
            260                 265                 270
Glu Glu Ile Trp Lys Ala Asp Arg Pro Gly Asn Ala Ala Trp Asn Leu
        275                 280                 285
Ala Glu Val Glu Phe Thr Cys His Phe Pro Leu Gln Val Ile Phe Glu
    290                 295                 300
Val Ala Phe Asn Gly Pro Lys Gly Gly Tyr Val Ala Leu Asp Asp Ile
305                 310                 315                 320
Ser Phe Ser Pro Val His Cys Gln Asn Gln Thr Glu Leu Leu Phe Ser
                325                 330                 335
Ala Val Glu Ala Ser Cys Asn Phe Glu Gln Asp Leu Cys Asn Phe Tyr
            340                 345                 350
Gln Asp Lys Glu Gly Pro Gly Trp Thr Arg Val Lys Val Lys Pro Asn
        355                 360                 365
Met Tyr Arg Ala Gly Asp His Thr Thr Gly Leu Gly Tyr Tyr Leu Leu
    370                 375                 380
Ala Asn Thr Lys Phe Thr Ser Gln Pro Gly Tyr Ile Gly Arg Leu Tyr
385                 390                 395                 400
Gly Pro Ser Leu Pro Gly Asn Leu Gln Tyr Cys Leu Arg Phe His Tyr
                405                 410                 415
Ala Ile Tyr Gly Phe Leu Lys Met Ser Asp Thr Leu Ala Val Tyr Ile
            420                 425                 430
Phe Glu Glu Asn His Val Val Gln Glu Lys Ile Trp Ser Val Leu Glu
        435                 440                 445
Ser Pro Arg Gly Val Trp Met Gln Ala Glu Ile Thr Phe Lys Lys Pro
    450                 455                 460
Met Pro Thr Lys Val Val Phe Met Ser Leu Cys Lys Ser Phe Trp Asp
465                 470                 475                 480
Cys Gly Leu Val Ala Leu Asp Asp Ile Thr Ile Gln Leu Gly Ser Cys
                485                 490                 495
Ser Ser Ser Glu Lys Leu Pro Pro Pro Pro Gly Glu Cys Thr Phe Glu
            500                 505                 510
Gln Asp Glu Cys Thr Phe Thr Gln Glu Lys Arg Asn Arg Ser Ser Trp
        515                 520                 525
His Arg Arg Arg Gly Glu Thr Pro Thr Ser Tyr Thr Gly Pro Lys Gly
    530                 535                 540
Asp His Thr Thr Gly Val Gly Tyr Tyr Met Tyr Ile Glu Ala Ser His
545                 550                 555                 560
Met Val Tyr Gly Gln Lys Ala Arg Leu Leu Ser Arg Pro Leu Arg Gly
                565                 570                 575
Val Ser Gly Lys His Cys Leu Thr Phe Phe Tyr His Met Tyr Gly Gly
            580                 585                 590
Gly Thr Gly Leu Leu Ser Val Tyr Leu Lys Lys Glu Glu Asp Ser Glu
        595                 600                 605
Glu Ser Leu Leu Trp Arg Arg Arg Gly Glu Gln Ser Ile Ser Trp Leu
    610                 615                 620
Arg Ala Leu Ile Glu Tyr Ser Cys Glu Arg Gln His Gln Ile Ile Phe
625                 630                 635                 640
Glu Ala Ile Arg Gly Val Ser Ile Arg Ser Asp Ile Ala Ile Asp Asp
                645                 650                 655
Val Lys Phe Gln Ala Gly Pro Cys Gly Glu Met Glu Asp Thr Thr Gln
            660                 665                 670
Gln Ser Ser Gly Tyr Ser Glu Asp Leu Asn Glu Ile Glu Tyr
        675                 680                 685
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<210> 78
<211> 154
<212> PRT
<213> Homo sapiens

<400> 78

Met	Thr	Leu	Ser	Pro	Thr	Gln	Pro	Pro	Leu	Phe	His	Leu	Pro	Tyr	Val
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Gln	Lys	Cys	Phe	Ile	Pro	Thr	Val	Glu	Gln	Leu	Thr	Leu	Gly	Ile	Pro
			20					25					30		
Cys	Gln	Asn	His	Gly	Glu	Ile	Asp	His	Gly	Gln	Asp	Ile	Phe	Pro	Ala
		35					40					45			
Glu	Lys	Leu	Cys	His	Leu	Gln	Asp	Cys	Lys	Val	Asn	Leu	His	Arg	Ala
	50					55					60				
Ala	Cys	Gly	Glu	Cys	Ile	Val	Ala	Pro	Lys	Thr	Ser	Ser	Phe	Pro	Tyr
65					70					75					80
Cys	Gln	Gly	Thr	Cys	Leu	Thr	Leu	Asn	Ser	Glu	Leu	His	Gln	Ser	Asn
				85					90					95	
Phe	Ala	Leu	Lys	Val	Cys	Thr	Ile	Arg	Gly	Glu	Cys	Leu	Leu	Ile	Cys
			100					105					110		
Ser	Trp	Leu	Phe	Gln	Thr	Cys	Ser	Pro	Thr	Lys	Val	Ile	Leu	Phe	Ser
		115					120					125			
Leu	Thr	Val	Gln	Asp	Asp	Glu	Arg	Lys	Met	Ser	Val	His	Cys	Val	Asn
	130					135					140				
Ala	Ser	Leu	Ile	Glu	Lys	Cys	Gly	Cys	Ser						
145					150										

INTERNATIONAL SEARCH REPORT

Int[illegible] onal application No.
PCT/US01/13360

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :C07H 21/04; C12P 21/06; C12N 9/00, 1/20, 15/00

US CL :435/69.1, 183, 252.2, 320.1; 536/23.2

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/69.1, 183, 252.2, 320.1; 536/23.2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

BIOSIS, CAPLUS, MEDLINE, EMBASE, GENBANK, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A, P	CARNINCI, P et al. Normalization and subtraction of cap-trapper-selected cDNAs to prepare full-length cDNA libraries for rapid discovery of new genes, Genome Res., October 2000, Vol.10, No.10, pages 1617-1630, see enitre article.	1-7
A, P	WO 00/55350 A1 (HUMAN GENOME SCIENCES, INC.) 21 September 2000 (21-9-00).	1-7
A	WO 95/30428 A1 (HUMAN GENOME SCIENCES, INC.) 16 November 1995 (11-16-95).	1-7
A	US 5,830,744 A (ROSEN et al.) 03 November 1998 (11-03-98).	1-7

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
07 JULY 2001	02 AUG 2001
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer MANJUNATH RAO
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet) (July 1998)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/15560

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-7, SEQ ID NO:1 and 40

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/13360

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

1) Polynucleotide sequences with SEQ ID NOs 1 through 39.

2) Polypeptide sequences with SEQ ID NOs: 40-78.

The following claims are generic: Claims 1-7

The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the above polynucleotide and polypeptide sequences are patentably distinct from each other as they have different structure and function.